CORRELATIVE ASSESSMENT OF CLINICAL PROFILE WITH LABORATORY INVESTIGATIONS IN HEREDITARY MUSCLE DISORDERS

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CERTIFICATE

This is to certify that the dissertation entitled **"CORRELATIVE ASSESSMENT OF CLINICAL PROFILE WITH LABORATORY INVESTIGATIONS IN HEREDITARY MUSCLE DISORDERS"** is a bonafide original work of **DR.N.BALAMURUGAN,** in partial fulfillment of the requirements for D.M. Branch– I (Neurology) Examination of the Tamil Nadu Dr.M.G.R Medical University to be held in August 2013, under our guidance and supervision.

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DECLARATION

I hereby solemnly declare that this dissertation titled **"CORRELATIVE ASSESSMENT OF CLINICAL PROFILE WITH LABORATORY INVESTIGATIONS IN HEREDITARY MUSCLE DISORDERS"** was done by me in Institute of Neurology, Madras Medical college and Rajiv Gandhi Government General Hospital, Chennai -3, under the guidance and supervision of Prof. **S.BALASUBRAMANIAN,MD.,DM.,** Professor of Neurology, Institute of Neurology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai. This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirement for the award of D.M Degree Branch I (Neurology).

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CONTENTS

INTRODUCTION

Myopathies are disorders in which a primary functional or structural impairment of skeletal muscle exists.Muscle disorders are differentiated from disorders involving motor neurons,peripheral nerves or neuromuscular junction, by their characteristic clinical and laboratory features. Therefore, the approach to a patient with a suspected muscle disease is to determine the correct site of the lesion from history and physical examination. Once localized to the muscle, the next step is to identify whether the myopathy is due to a defect in the muscle channel, muscle structure, or a dysfunction in muscle metabolism. Subsequently the cause of the myopathy is to be determined.

In general, Muscle disorders are classified into hereditary and acquired disorders. Hereditary muscle disorders have classical age at onset, inheritance pattern, clinical profile, pattern of involvement and distinct laboratory features which helps in the diagnosis. This will help to decide on management and prognostication issues. It is also essential to identify treatable acquired muscular disorders and to differentiate them from hereditary muscle disorders. We undertook this study of hereditary muscle disorders to identify the clinical patterns and laboratory findings in these conditions and study the correlation between them, which will help in recognizing them early for adequate management with rehabilitation measures and for prognostication.

AIMS AND OBJECTIVES

The aim of the study is,

1. To study the demographic profile in Hereditary muscle disorders.

2. To study the clinical spectrum of hereditary muscle disorders.

3. To Assess the correlation between the clinical and investigational profile in Hereditary muscle disorders.

REVIEW OF LITERATURE

A CLINICAL APPROACH TO THE PATIENT WITH SUSPECTED MYOPATHY

CLINICAL EVALUATION

The approach to a patient with suspected myopathy is by obtaining a thorough history for preliminary diagnosis and a detailed physical examination, including the pattern of muscle weakness, which provides further information in determining the correct diagnosis.[1] The laboratory studies then, play a confirmatory diagnostic role.

Based on the symptoms and signs,the clinical approach in a patient includes the following steps

(1) Symptoms and Signs Associated With Myopathies

1. Negative

- Weakness
- Fatigue
- Exercise intolerance
- Muscle atrophy

2. Positive

- Myalgias

- Cramps
- Contractures
- Myotonia
- Myoglobinuria

Symptoms and signs of muscle disease are divided into negative complaints such as weakness, exercise intolerance, fatigue, and muscle atrophy, and positive complaints such as myalgias, cramps, contractures, myoglobinuria, myotonia and muscle stiffness.[3]

- Weakness is the most common negative symptom reported by a patient with muscle disease.The proximal muscle weakness is the most common type of weakness in a myopathic disorder.Less commonly,patients with myopathies can complain of distal weakness . Some myopathies may also result in cranial muscle weakness,resulting in dysarthria,dysphagia, or ptosis.

- Fatigue is a much less useful nonspecific negative symptom, and reflects a patient's cardiopulmonary status, level of conditioning, overall health, sleeping habits, or emotional state. Abnormal fatigability after exercise can result from certain metabolic and mitochondrial myopathies. Myalgia, is another nonspecific (positive)symptom of some myopathies.Myalgias may be episodic

(metabolic myopathies) or nearly constant (inflammatory muscle disorders).

- A specific type of muscle pain is the involuntary muscle cramp, lasting from seconds to minutes and are usually localized to a particular muscle region.They are usually benign, occurring frequently in normal individuals,and are not a feature of a primary myopathy. Cramps are characterized by rapidly firing motor unit discharges,which can be demonstrated on needle EMG. Cramps can occur with dehydration,hyponatremia, azotemia, and myxedema and in disorders of the nerve or motor neuron (especially amyotrophic lateral sclerosis). Contractures differ from cramps in that they usually last longer and are electrically silent with needleEMG.

- Myotonia is the phenomenon of impaired relaxation of muscle after forceful voluntary contraction , commonly involving the hands ,eyelids and is due to repetitive depolarization of the muscle membrane.Patients may complain of muscle stiffness resulting in difficulty releasing their handgrip after a handshake or opening their eyelids if they forcefully shut their eyes. Myotonia classically improves with repeated exercise but the patients with paramyotonia congenita demonstrate ‘‘paradoxical myotonia’’ in which symptoms are typically worsened by repeated muscle contractions. Exposure to cold results in worsening of both myotonia and paramyotonia.

- Myoglobinuria is a relatively uncommon manifestation of muscle disease,is caused by the release of myoglobin from muscle during

periods of rapid muscle destruction (rhabdomyolysis) and can result in renal failure due to acute tubular necrosis..Recurrent myoglobinuria is usually due to an underlying metabolic myopathy,but isolated episodes occurring after unaccustomed exercise, are frequently idiopathic.

(2)Temporal evolution

It is important to determine the onset, duration, and evolution of the patient's symptoms and signs of muscle disease.Onset of symptoms in Duchenne muscular dystrophy is usually by age 3, whereas most facioscapulohumeral and limb-girdle muscular dystrophies begin in adolescence or later. Dermatomyositis occurs in children and adults,polymyositis occurs rarely in children but at any decade in the adult years and inclusion body myositis occurs most commonly in the elderly.

It is important to determine the duration and evolution of the disease. Muscle disorders with (1)constant weakness include muscular dystrophies, inflammatory myopathies and (2) episodic weakness with normal strength interictally include periodic paralysis, metabolic myopathies. The episodic disorders have acute weakness that returns to normal strength within hours or days. The disorders with constant weakness can be (1) acute or subacute progression as in some

inflammatory myopathies, (2) chronic slow progression over years as in most muscular dystrophies or (3) nonprogressive weakness with little change over decades as in congenital myopathies.

(3) Family history

- Since many muscle disorders are inherited, obtaining a thorough family history is clearly of great importance in making a correct diagnosis. A detailed family tree is necessary for evidence of autosomal dominant, autosomal recessive, or X-linked patterns of transmission. Identifying a hereditary pattern is also of importance in providing appropriate genetic counseling.

(4) Precipitating factors that trigger episodic weakness or myotonia

A history of precipitating factors that trigger or exacerbate symptoms should be explored.

- Illegal drug or prescription medication use
- Exercise induced Weakness, pain or myoglobinuria might suggest the possibility of a glycolytic pathway defect.
- Fever with episodes of weakness would be supportive of a diagnosis of carnitine palmityl transferase deficiency.
- Periodic paralysis is characteristically provoked by exercise or ingestion of a carbohydrate meal followed by a period of rest.

- cold exposure precipitating muscle stiffness occurs in Patients with paramyotonia congenita.

(5) Associated systemic symptoms or signs

Involvement of organs or tissues other than muscle may also provide clues in making the appropriate diagnosis.

- Cardiac disease may be associated with myotonic dystrophy, Duchenne or Becker muscular dystrophies,LGMD1B (laminopathy), LGMD2I(fukutin-related protein),LGMD2C–2F(sarcoglycanopathies), LGMD2G (telethoninopathy),Emery-Dreifuss muscular dystrophy, and Andersen syndrome.

- Respiratory failure may be the presenting symptom of myotonic dystrophy,centronuclearmyopathy, nemaline myopathy, or acid maltase deficiency.

- Hepatomegaly may occur in myopathies with deficiencies in acid maltase, debranching enzyme and carnitine.

- The presence of cataracts,frontal balding, and mental retardation strongly suggests the diagnosis of myotonic dystrophy.

- Dysmorphic features may be associated with the congenital myopathies.

- The presence of a rash is extremely helpful in confirming the diagnosis of dermatomyositis.

- Contractures developing early in the course of the disease occurs in LGMD1B(laminopathy), Emery-Dreifuss dystrophy and Bethlem myopathy.

- Evidence of diffuse systemic disease can indicate amyloidosis, sarcoidosis, endocrinopathy,collagen–vascular disease,infectious disease, or a mitochondrial disorder.

(6) Distribution of weakness

To determine the distribution of weakness, muscle strength is assessed using the expanded Medical Research Council (MRC) of Great Britain grading scale of 0 to 5.[2]

(7) Muscle atrophy

- Atrophy of proximal limb muscles is common in most chronic myopathies.

- Atrophy in specific groups that correspond to severe weakness in the muscles, provide additional diagnostic clues.

    a. Atrophy of the periscapularmuscles with winging of scapula occurs in facioscapulohumeral dystrophy.

    b. Scapular winging is also occurs in LGMD1B (laminopathy), LGMD2A (calpainopathy),and LGMD2C–2F (sarcoglycanopathies).

    c. In inclusion body myositis Selective atrophy of the quadriceps muscles and forearm flexor muscles occur.

d. Atrophy of the anterior or posterior lower extremity compartments occur in Distal myopathies.

(8) Muscle hypertrophy

a. Muscle hypertrophy occurs in conditions such as myotonia congenita, amyloidosis, sarcoidosis,and hypothyroid myopathy.

b. Calf muscles hypertrophy occurs in Duchenne and Becker dystrophy, LGMD2C–2F (sarcoglycanopathies)and LGMD2I (fukutin-related protein).

c. In LGMD2G (telethoninopathy),50% of the patients will show calf hypertrophy and 50% will demonstrate calf atrophy.

d. Focal muscle enlargement can also be due to a neoplastic or inflammatory process, ectopic ossification, tendon rupture, or partial denervation.

PATTERN-RECOGNITION APPROACH TO MYOPATHIC DISORDERS

Myopathies usually occurs in any one of the following six patterns of weakness which aids in the diagnosis of specific muscle disorders.[4]

- Pattern 1: Proximal Limb-Girdle Weakness

    - The most common pattern is symmetrical weakness involving predominantly the proximal muscles of the legs and arms(limb-girdle).The distal muscles,neck extensor and flexor muscles are usually involved, but to a much lesser extent.This pattern of weakness is seen in most hereditary and acquired myopathies and therefore is the least specific in arriving at a particular diagnosis.

- Pattern 2: Distal Weakness

    - This pattern of weakness predominantly involves the distal muscles of the upper or lower extremities (anterior or posterior compartment muscle groups).Depending on the diagnosis and severity of disease, proximal muscles may also be affected. The involvement is usually symmetrical. (Nonaka, Miyoshi etc.)

- Pattern 3: Proximal Arm/Distal Leg Weakness

    - This pattern of weakness affects the periscapular muscles of the proximal arm and the anterior compartment muscles of the distal lower extremity (scapuloperoneal).When the weakness is asymmetrical with associated facial weakness, it

is suggestive of a diagnosis of facioscapulohumeral dystrophy.

- Other hereditary myopathies associated with a scapuloperoneal distribution of weakness include scapuloperoneal dystrophy, Emery-Dreifuss dystrophy,LGMD1B, LGMD2A, LGMD2C–2F, congenital myopathies, and acid maltase deficiency.

- Pattern 4: Distal Arm/Proximal Leg Weakness

  - This pattern involves the distal forearm muscles (wrist and finger flexors) and proximal leg weakness involving the knee extensors (quadriceps) and is often asymmetrical between the two sides. This pattern is pathognomonic for inclusion body myositis (IBM).

- Pattern 5: Ptosis With or Without Ophthalmoplegia

  - Ptosis with ophthalmoplegia and dysphagia occurs in oculopharyngeal muscular dystrophy. Ptosis with ophthalmoplegia but without dysphagia occurs in mitochondrial myopathies.ptosis with facial weakness ,without ophthalmoplegia occurs in myotonic dystrophy.

- Pattern 6: Prominent Neck Extensor Weakness

  - This pattern is also called as‘‘dropped head syndrome’’ occurs in isolated neck extensor myopathy and other neuromuscular diseases like amyotrophic lateral sclerosis and myasthenia gravis.

LABORATORY APPROACH IN THE EVALUATION OF A SUSPECTED MYOPATHY

1) Creatine Kinase

- The most useful laboratory study in patients with a suspected myopathy is creatine kinase.[5] The CK is elevated in most of the muscle diseases but may be normal

- in slowly progressive muscle disorders. The degree of elevation gives clue to the diagnosis of specific myopathies.

- Marked elevation of CK occurs in Duchenne dystrophy(10-100 times normal),LGMD1C(caveolinopathy), LGMD2A(calpainopathy), and LGMD2B (dysferlinopathy).

- In myopathies with severe muscle wasting,steroid administration,collagen diseases,hyperthyroidism or alcoholism,the CK levels may be normal or low.

- Other than in myopathies,CK may be seen slightly elevated in motor neuron disease, Guillain-Barre syndrome or chronic inflammatory demyelinating neuropathy, hypothyroidism, hypoparathyroidism, seizures,muscle trauma(falls, intramuscular or subcutaneous injections, EMG studies), viral illnesses or strenuous exercise.

- Race and gender also affect serum CK levels (above the normal range in some African American individuals and in males).[5]

- CK isoenzymes are nonspecific,CK-MB are elevated in both cardiac and muscle disorders.CK-MM fraction is increased in myopathies.

- Other enzymes such as aldolase,aspartate aminotransferase(AST),alanine aminotransferase(ALT), and lactate dehydrogenase(LDH) may be slightly elevated in myopathies.

2) Electrophysiological Studies

- Electrophysiology (nerve conduction studies and EMG), is a part of the routine investigation in a patient with a suspected myopathy. These studies confirm the localization as muscle and not the Anterior horn cell, nerve or neuromuscular junction.

- In patients with myopathy, the nerve conduction studies (both motor and sensory conduction studies) are normal.

- Needle EMG study shows myogenic pattern (short duration, small-amplitude motor units with early recruitment, complete interference pattern) in muscle disorders.[6]

3) The Muscle Biopsy

- Muscle biopsy is an important step in establishing the diagnosis in patients with suspected myopathy.[7]

- Open or closed(needle or punch) biopsy procedure is needed to obtain a muscle specimen.

- Selection of the appropriate muscle to biopsy is more important.Muscles that shows MRC grade 4 strength are biopsied and is avoided in severely involved muscles or in muscles recently subjected to needle EMG study.

- In the upper extremities,the muscle of choice is the biceps; in the lower extremities, the best choice is the vastus lateralis.

- Sometimes an imaging like muscle ultrasound,computed tomography, or magnetic resonance imaging is used to guide selection of the suitable muscle for biopsy.

- Light microscopy, electron microscopy,biochemical studies, and immune staining are used to analyse the specimens.

- Myopathic features include internalised nuclei, small and large round fibers, split fibers, degenerating and regenerating fibers. Chronic myopathies show increased connective tissue and fat.

- The hematoxylin and eosin (H&E) and modified Gomori trichrome are useful for routine histology. The MGT stain is helpful in detecting ragged red fibers, which suggests a mitochondrial disorder.

- The myosin adenosine triphosphatase stains (alkaline pH 9.4 and acidic pH 4.3 and 4.6)are used for identifying fiber types. Type 1 fibers stain lightly at alkaline and darkly at acidic pH levels, whereas the Type 2 fibers stain darkly at alkaline and lightly at acidic pH levels. Normally, twice as many type 2 as type 1 fibers are identified. A nonspecific type 1 fiber predominance is common

in a number of myopathies. Oxidative enzyme stains (nicotinamide adenine dinucleotide[NADH] dehydrogenase, succinate dehydrogenase (SDH), cytochrome-c oxidase) are used to diagnose myofibrillar and mitochondrial abnormalities. Acid and alkaline phosphatase reactions for necrotic and regenerating fibers, respectively.

- Periodic acid-Schiff (PAS) stain, oil red O stain and a Congo red stain are ued for diagnosing glycogen storage diseases, lipid storage diseases and amyloid deposition respectively.

- Qualitative biochemical enzymes stains can be done for myophosphorylase(McArdle's disease), phosphofructokinase (PFK deficiency), and myoadenylate deaminase (MAD deficiency).

- immunohistochemical techniques are used to detect muscle proteins that are deficient in some muscular dystrophies(eg, dystrophin in Duchenne and Becker dystrophy) or to identify products that are increased in certain inflammatory myopathies (eg. membrane attack complex in dermatomyositis).

- Electron microscopy is used to detect the ultrastructural components of muscle fibers and aids in the diagnosis of some congenital myopathies, mitochondrial disorders.

- Western blot analysis from muscle tissue can be performed for certain muscle proteins (dystrophin assays in Duchenne or Becker dystrophy).

4) Molecular Genetic Studies

- The specific molecular genetic defect is now known for a large number of hereditary myopathies, and mutations can be identified by peripheral blood DNA analysis.

- Molecular genetic testing now eliminates the need for muscle biopsy in many myopathies. This is also helpful for detecting carrier status and for prenatal diagnosis.

5) Other blood tests that are helpful to rule out the acquired myopathies include thyroid function tests, parathyroid hormone levels and human immunodeficiency virus (HIV). In patients with an inflammatory myopathy, serological tests for other autoimmune conditions like systemic lupus erythematosus, rheumatoid arthritis, and other immunological markers (eg, Jo-1 antibodies) may be useful. A urine analysis can be done to detect the presence of myoglobinuria, if the urine tests positive for blood and no red blood cells are found.

6) Forearm exercise test

It is done in patients with a suspected metabolic myopathy. The test is done by asking the patient to do isometric contractions using a handgrip dynamometer for a period 1 minute. A resting blood sample for venous lactate and ammonia is obtained at baseline and subsequently at 1, 2, 4, 6,and 10 minutes after the completion of exercise. Normally a

threefold rise in lactate level is obtained. The absence of elevation of serum lactate after exercise is seen in phosphofructokinase deficiency, myophosphorylase deficiency and reduced in phosphoglycerate mutase deficiency. Forearm testing is normal in all disorders of fat metabolism and also in some glycolytic disorders with fixed muscle weakness, such as acid maltase deficiency.

This pattern-recognition approach to myopathy is helpful in narrowing down the differential diagnosis and therefore minimizing the number of laboratory studies that must be ordered to confirm the diagnosis. Careful consideration of the distribution of muscle weakness and attention to these common patterns of involvement in the context of other aspects of the neurological examination and laboratory evaluation will usually lead to a timely and accurate diagnosis.

Muscle disorders are broadly classified as,[8]

1. Hereditary

- Muscular dystrophies
- Myotonias
- Channelopathies
- Congenital myopathies

- Metabolic myopathies
- Mitochondrial myopathies

2.Acquired

- Inflammatory myopathies
- Endocrine myopathies
- Myopathies associated with
- other systemic illness
- Drug-induced myopathies
- Toxic myopathies

MUSCULAR DYSTROPHIES

DUCHENNE MUSCULAR DYSTROPHY (DMD)

It is one of the most common and severe of the muscular dystrophies, affecting approximately one in 3,300 male live-births.[9] It is transmitted as an X-linked recessive trait. DMD is caused by the mutation in DMD gene which encodes a 427 kd protein called dystrophin. dystrophin connects the cytoskeletal protein (actin) to extracellular connective tissue matrix through transmembrane proteins(dystroglycans and sarcoglycans) and thus provides structural support to the sarcolemma

during muscle stretch. So, the absence of dystrophin results in damage to the muscles.

The disease onset is in early childhood, usually before the age of 4 years and always before the age of 10 years. Walking is delayed in about half of the patients and due to severe proximal limb weakness they develop waddling gait and compensatory lumbar lordosis. In rising from the floor, affected children "climb up" their legs to the erect position (Gower's manoeuvre). Muscle enlargement, the pseudohypertrophy (calf) is often present from birth.Progression may vary, but by the age of 12 or 13 years the ability to walk is lost.Patients can have low IQ, cardiomyopathy. Most patients die before the age of 20 due to pulmonary or cardiac failure.

Elevated serum enzymes, especially CPK(10-100 times normal) and LDH. electromyography showing myopathic pattern. Muscle biopsy shows increased variation of fibre size, presence of large 'opaque' or 'hyaline' fibres, local areas of degenerating and regenerating fibres, increased number of internal nuclei and infiltration of fat and connective tissue. Positive family history is helpful. In doubtful cases the diagnosis can be confirmed by dystrophin immunoblotting. Carrier detection as well as prenatal diagnosis is now possible.

Treatment

No specific therapy is available, Prednisolone (0.75 mg/kg/day) is effective in increasing muscle strength, function and slowing of the rate of deterioration.[10] Exercises are encouraged and continued as long as possible. Corrective surgery is considered in slowly progressive cases. Novel treatments are myoblast transfer and direct gene replacement utilising modified viral vectors. Genetic counselling is offered to the affected family.

BECKER MUSCULAR DYSTROPHY (BMD)

This is also transmitted as an X-linked trait, with an incidence of about 10 per cent of DMD. Both DMD and BMD are due to genetic defects at the same locus on the X-chromosome, Xp2.[12] They are virtually identical to those of DMD but the onset is usually after the age of 5 years. Most patients are still able to walk beyond the age of 12 and often into adolescence and adult life; death usually occurs between the third and fifth decades, and almost never before the age of 20. Mental retardation is not as common as in DMD, and electrocardiogram abnormalities are unusual. As in DMD, hypertrophy of the calves is often pronounced from childhood, and serum CPK is markedly increased even before weakness becomes manifest. EMG and muscle biopsy findings are similar to those of DMD but abnormalities tend to be milder. Treatment is similar to that of DMD.

EMERY DREIFUSS DYSTROPHY

This is a childhood-onset disease with multiple contractures inherited in X-linked recessive manner, associated with cardiomyopathy. It affects predominantly the humeroperoneal muscles. It is slowly progressive. Sudden death due to abnormalities of the conducting system of the heart is not uncommon. Serum CPK is slightly increased. ECG shows varying degrees of atrioventricular block. Cardiac pacemaker implantation may be needed.

Limb-Girdle Muscular Dystrophies

There is a large group of patients with muscular dystrophy who do not fit into the Duchenne/Becker, facioscapulohumeral, or scapuloperoneal categories. Children of both sexes in this group lack the hypertrophy of calves and other muscles; adults with late-onset forms have either pelvic or shoulder girdle involvement or both, and their facial muscles are spared. The inheritance is variable but the autosomal recessive forms are the most common. Either the shoulder girdle or pelvic girdle muscles may be first affected. Weakness and atrophy may become evident during either late childhood or early adult life and spread from shoulders to hips or vice versa.

The later the onset of these disorders, the more likely that the course will be benign. In these lesser-affected patients the EMG is myopathic, the CK values are only moderately elevated and may be normal. More severe cases can have greatly elevated CK levels. Cardiac involvement is infrequent, and mental function is normal but there are exceptions including in cases of laminin A/C mutations (type 1B), *FKRP* (fukutin-related protein mutation) mutations (type 2I), and in the sarcoglycanopathies.

The limb-girdle dystrophies are classified as LGMD1 for the autosomal dominant types and LGMD2 for the recessive types, and further subclassified based on the specific genotype.[13] At least 11 forms of autosomal recessive (LGMD type 2) and 6 forms of autosomal dominant (LGMD type 1) limb-girdle dystrophies have been defined, with some specific clinical phenotype, most with an identifiable mutation and a protein that in most cases turns out to be a constituent of the muscle membrane.

Facioscapulohumeral Muscular Dystrophy

This is a slowly progressive dystrophy involving primarily the musculature of the face and shoulders, often with long periods of nearly

complete arrest. The pattern of inheritance is usually autosomal dominant.[14]

The age of onset is usually between 6 and 20 years, but cases beginning in early adult life are occasionally encountered. Weakness and atrophy of the involved muscles are the major physical findings; pseudohypertrophy occurs only rarely and is slight. As a rule, the first manifestations are difficulty in raising the arms above the head and winging of the scapulae, although bifacial weakness may have initially attracted attention, even in early childhood.The lips have a peculiar looseness and tendency to protrude.

The lower parts of the trapezius muscles and the sternal parts of the pectorals are almost invariably affected. By contrast, the deltoids may seem to be unusually large and strong, an appearance that may be mistaken for pseudohypertrophy. The scapulae are winged and elevated ("angel-wing" appearance), and the clavicles stand out. Usually the biceps waste less than the triceps, and the brachioradialis muscles even less, so that the upper arm may be thinner than the forearm ("Popeye" effect). Pelvic muscles are involved later and to a milder degree, giving rise to a slight lordosis and pelvic instability. The pretibial muscles weaken, and foot-drop is added to the waddling gait. The Beevor sign, an upward

movement of the umbilicus on flexing the neck as a result of weakness of the lower abdominal muscles, is common.

Initially, and even throughout the course, the muscular weakness may be asymmetrical (winging of only one scapula). Many of the patients with milder degrees of this form of dystrophy are unaware that they have the disease. At any point, the disease may become virtually arrested. Nevertheless, 15 to 20 percent of patients eventually require a wheelchair. Mental function is normal. Exudative retinal detachment (Coats disease) and other retinal abnormalities are an integral part of the disease. Serum CK values are normal or slightly elevated.

Scapuloperoneal Muscular Dystrophy

Mutation in the *FHL-1* gene on the X-chromosome results in a distinctive pattern of progressive muscular weakness and wasting that involved the muscles of the neck, shoulders, and upper arms, and of the anterior tibial and peroneal groups, causing severe foot-drop. The onset of symptoms is in early or middle adult life, with difficulty in walking because of bilateral foot-drop; symptoms referable to scapulohumeral involvement came later. Progression was slow, and none of the patients became severely incapacitated. In addition to the nonspecific histologic features of muscular dystrophy, some fibers contained eosinophilic

hyaline inclusions and rimmed vacuoles. It is now clear that there is genetic heterogeneity in these cases.

MYOTONIC DYSTROPHY

This is transmitted as an autosomal dominant disorder with varying degree of expression. It involves not only muscles but also other systems. An unstable mutant gene on the long arm of chromosome 19 (19q 13.3) with an increased number of trinucleotide CTG repeats is responsible and encodes a protein-myotonin protein kinase.[15]

The age of onset in usually between 20 and 50 years. The clinical features include muscle weakness, predominantly in distal groups, associated with wasting and myotonia. Multisystem involvement is manifested by cardiopathy (ECG abnormalities and congestive failure in late stages), cataract, mental retardation, hypogonadism and other endocrine dysfunctions, and frontal balding.[16] Atrophy of the temporalis, masseter and facial muscles gives rise to a typical "hatchet-faced" appearance. The speech is often dysarthric along with swallowing difficulty due to palatal, pharyngeal and tongue muscle involvement. Some patients may have external ophthalmoplegia in the early stages.

By 5 years of age, myotonia can be demonstrated either by percussion over the tongue, thenar eminence and wrist extensor muscles or by delayed handgrip relaxation, though it may be generalised.Affection of intercostal muscles and diaphragm leads to alveolar hypoventilation and respiratory insufficiency. Malabsorption syndrome may occur due to involvement of gastrointestinal smooth muscles.

In severe cases there is a high incidence of cataracts, testicular atrophy, premature balding, cardiac conduction defects and diabetes mellitus. Mental retardation is common. Death occurs by the age of 50 years. There is a tendency to anticipation in successive generations. Congenital myotonic dystrophy is seen in approximately 25% of infants of affected mothers. It is a more severe form of the disease characterised by weakness of facial and bulbar muscles with neonatal respiratory insufficiency and impaired intelligence.

The diagnosis of myotonic dystrophy is based on clinical features in most cases. Serum CPK level is usually normal or minimally elevated. EMG is pathognomonic, showing high-frequency waxing and waning discharges and a myopathic pattern. Muscle atrophy, especially of type I fibres, in more than 50% of cases with increased numbers of central nuclei, ring fibres and sarcolemmal masses can be seen on muscle biopsy.

Treatment

Phenytoin (5 mg/kg/d) is the preferred agent for patients who need antimyotonia drugs. Quinine (300-600 mg bid or tid) and procainamide (beginning with low dose and increasing slowly up to 4-6 g/d) are avoided in the elderly as they may affect cardiac conduction. The

calcium-channel blocker nifedipine has been reported to be effective in resistant cases.

MYOTONIA CONGENITA (THOMSEN'S DISEASE)

- This autosomal dominant disease is characterised by myotonia which is more noticeable on starting activity, especially after prolonged rest. Interestingly, the myotonia is exacerbated by cold and can be "worked off" with continuing activity. There may be hypertrophy of muscles diffusely. Strength is generally well preserved.Specific decrease in chloride conductance causes increased membrane resistance. This is seen in electrophysiologic studies of intercostal muscle biopsies.

- The autosomal recessive variety has more pronounced muscle hypertrophy than that of the dominant form, and there is usually weakness.

- Serum CPK level is normal and EMG shows myotonic discharges. Biopsy of muscles reveals normal architecture. Mexiletine, quinine, procainamide and diphenylhydantoin are useful in control of symptoms.

PROXIMAL MYOTONIC MYOPATHY (PROMM)

i) autosomal dominant inheritance, ii) proximal muscle weakness, iii) cataract, iv) myotonia mainly of the hand and proximal muscle.

The onset is usually between the ages of 20 and 40 years. It runs a slowly progressive course without significant atrophy. Non-specific myopathy is seen on muscle histology.

PERIODIC PARALYSIS AND CHANNELOPATHIES

Periodic paralysis is now included as a disorder of ion channels, popularly called "the channelopathies". Four types of ion channels have been identified till date and all of them seem to have at least one clinically recognised disorder.

- **Sodium channel disorders-**Hyperkalaemic periodic paralysis ,Normokalaemic periodic paralysis, Paramyotonia congenita Myotonia fluctuans, Myotonia permanens ,Acetazolamide-responsive myotonia.

- **Calcium channel disorders-** Central core disease ,Malignant hyperthermia, Hypokalaemic periodic paralysis.

- **Chloride channel disorders-** Myotonia congenital(Thomsen's disease), Generalised myotonia(Becker).

- **Potassium channel disorders-** Episodic ataxia-myotonia syndrome, Long Q-T syndrome.

Table – 1

Important features of the periodic paralysis

		Hypo-kalaemic	Normo-kalaemic	Hyper-kalaemic
•	Channel defect	DHP Ca+++	Na+	Na+
•	Age of onset	2nd to 3rd decade	1st decade	1st decade
•	Precipitating factor			
	Fasting	-	-	+
	Carbohydrate load	+	-	-
	Potassium load	-	±	++
	Cold	+	+	++
	Emotional stress	+	±	++
	Pregnancy	+	-	++
•	Cranial muscle involvement	+	±	-
•	Permanent myopathy	+	+	+
•	Serum CPK during attack			
•	Treatment	Large-dose KCl, with acetazola-mide in the intervening period	Large doses of Na+	Large doses of glucose with insulin; large intervening carbohydrate diet

- - Absent; + present; ± may be present; ++ significantly present; raised.

MITOCHONDRIAL DISORDERS

A dozen mitochondrial DNA mutations have been associated with neuromuscular, psychiatric, ophthalmologic, endocrine and gastrointestinal disorders. Basically, mitochondrial myopathy is considered to be a disorder of muscles with abnormal structure, size, form

and number of mitochondria in the muscle. Ragged red fibres, containing peripheral and intermyofibrillar accumulations of abnormal mitochondria seen with the modified Gomori trichrome stain, are the morphological hallmark of these disorders. For a simplified understanding, mitochondrial disorders mainly constitute infantile lactic acidosis, progressive external ophthalmoplegia, the Kearns-Sayre syndrome, myopathies and encephalomyopathies.

The Kearns-Sayre syndrome (KSS) is characterised by progressive external ophthalmoplegia and pigmentary retinopathy with onset before the age of 20 years, with one or more of the following features: ataxia, increased cerebrospinal fluid protein concentration (> 1 g/L) and cardiac conduction defects. Other features may include diabetes, hypoparathyroidism, short stature and deafness.

MERRF syndrome: Myoclonic epilepsy, encephalo-myopathy and ragged red fibres constitute the MERRF syndrome. This disorder has a maternal pattern of inheritance and affects complex IV of the respiratory chain.

MELAS syndrome: Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes constitute this syndrome. It has maternal inheritance and affects complex I.

Treatment of these disorders is disappointing. Steroids and respirator chain co-factors such as ubiquinone, menadione and ascorbic acid have been tried with variable results.

DISORDERS OF GLYCOGEN METABOLISM

Glycogen metabolism influenced by specific enzyme deficiencies gives rise to a number of glycogen storage diseases involving the skeletal muscles chiefly, with or without other tissues. They are transmitted as an autosomal recessive trait and muscle involvement is seen in types II, III, IV, V and VII.

Type II glycogen storage disease (acid maltase deficiency - AMD) is manifested either as generalised rapidly progressive and invariably fatal disease of infancy (Pompe's disease) or as a more benign neuromuscular disorder in childhood or adult life. The defect can be documented in muscles or cultured skin fibroblasts or body fluids.

Type III glycogen storage disease (debranching enzyme - amylo 1,6, -glucosidase deficiency): Skeletal muscle and liver involvement are the important manifestations of the disease. Genetic heterogeneity is seen in a number of cases. During the first month of life the infant fails to thrive and shows hepatomegaly. Hypotonia and proximal muscle weakness are detected on examination. Easy fatiguability, exercise

intolerance, muscle cramps, ketosis and hypoglycaemia may be seen in some cases. Hepatomegaly may resolve spontaneously by adolescence with normal development despite persistent enzyme defect.

Type IV glycogen storage disease (branching enzyme amylo 1,4-1,6 trans-glucosidase deficiency) is an autosomal recessive disorder. The clinical picture is characterised by progressive cirrhosis and chronic hepatocellular failure causing death in childhood. Muscle hypotonia and wasting are found in many cases. Small deposits of polysaccharide with a finely granular and filamentous structure are seen in electron microscopy of muscle biopsy.

Type V glycogen storage disease (myophosphorylase deficiency, McArdle's disease) is an inherited autosomal recessive disorder but with a 3:1 predominance in affected males. Intolerance to strenuous exercise is the dominant clinical feature along with pain, stiffness and weakness of exercising muscles which is relieved by rest. The early childhood and adolescent varieties are characterised by increased fatiguability, while in the late-onset cases severe muscle cramps and myoglobinuria may occur. Progressive muscle weakness and wasting gradually dominate the clinical picture with increasing age while myoglobinuria diminishes in course of time. Serum lactate fails to rise after forearm ischaemic exercise. The

diagnosis is confirmed by demonstration of glycogen in muscle histology and deficiency of phosphorylase in muscles histochemically and biochemically.

Type VII glycogen storage disease (phosphofructokinase deficiency) is an autosomal recessive disorder affecting the rate limiting enzyme of glycolysis and results in complete block of the glycolytic pathway. The clinical picture is similar to that of myophosphorylase deficiency in many aspects; exercise intolerance, cramps, myoglobinuria and progressive weakness occur in a few patients.

DISORDERS OF LIPID METABOLISM

Deficiences of carnitine and carnitine palmityl transferase give rise to muscle disorders affecting lipid metabolism.

Carnitine deficiency

The *myopathic carnitine deficiency* is an autosomal recessive disorder with a normal serum carnitine level while carnitine concentration in muscle is decreased due to a defect in the active transport mechanism. Weakness, especially of the proximal limb, trunk and neck muscles starting in childhood is the usual clinical picture. Rapid worsening with severe respiratory muscle weakness leading to ventilatory failure may occur. Serum CPK is raised and the EMG shows non-specific myopathic

features. Innumerable lipid droplets accumulate in type I fibres and appear as empty spaces reacting with stains for neutral fat. Administration of carnitine orally may result in some improvement while prednisolone may give dramatic response in some patients.

Carnitine palmityltransferase (CPT) deficiency

The clinical picture of CPT deficiency is dominated by myoglobinuria after exercise, more so in cold weather, after fasting or ingestion of fatty foods; occasionally acute renal failure ensues.

Transmitted as an autosomal recessive trait the patients are normal on clinical examination except during episodes of myoglobinuria.During an attack, muscle cramps, weakness and dark urine are presenting features which develop about 1-2 hours after exercise and last for 1 or 2 days. Muscle enzymes are raised during an attack. There is normal rise of lactate in ischaemic forearm exercise test. Virtually no ketone body formation takes place on fasting. Lipid droplets are found in type I muscle fibres and deficiency of CPT is observed in muscle as also in liver, leucocytes, platelets and in cultured skin fibroblasts.

Myoadenylate deaminase deficiency

It is an inherited disorder with males and females being equally affected. Fatigue, weakness, muscle cramps and soreness are experienced

following exertion. Though weakness is more pronounced in limb muscles, muscles of the trunk and chest may show variable involvement; characteristically the face and eye muscles are spared. In 50% of cases mild muscle weakness, atrophy, and tenderness on palpation may be found. Myoglobinuria has never been documented and fixed weakness has been noted in very few patients. Serum CPK is mildly raised and complex polyphasic units, positive sharp waves and low-amplitude action potentials are found on EMG. The lactate-ammonia exercise ratio is below 4% in affected individuals

The Distal Muscular Dystrophies :

Included in this group are several slowly progressive distal myopathies with onset principally in adult life. Weakness and wasting of the muscles of the hands, forearms, and lower legs, especially the extensors, are the main clinical features. Several types of distal dystrophies are inherited as autosomal dominant traits which includes Welander distal dystrophy, Tibial muscular dystrophy, Scapuloperoneal dystrophy, Desmin myopathy ,Gower-Laing, Markesbury-Griggs. The autosomal recessive types include Miyoshi myopathy, Nonaka myopathy with rimmed vacuoles (familial IBM).[1]

MATERIAL AND METHODS

Study Centre:

- Institute of Neurology,Madras Medical College,Chennai

Study design:

- Cross sectional study

Study period:

- July 2012 to February 2013(8 months)

Study Sample:

- 44 patients (Males-32,Females-12)

Inclusion criteria:

- Patients with clinical features suggestive of Hereditary muscle disorders

Exclusion criteria:

The following patients are excluded from the study,

- Patients with clinical features,electrodiagnostic tests (NCV/EMG) suggestive of neuropathies or neuromuscular junction disorders.
- Patients with features suggestive of drug-induced myopathies.
- Patients with features suggestive of toxic myopathies.

- Patients with features suggestive of Endocrine myopathies.
- Patients with features suggestive of myositis (infective/inflammatory).
- Patients with features of myopathy associated with other systemic illness.

Clinical Evaluation:

Clinical evaluation of all patients were done with,

- ❖ Detailed history taking
- ❖ Clinical examination
    i. General Examination with details about the presence of contractures,skeletal deformities,etc.
    ii. CNS Examination which included higher mental functions,cranial nerves, spinomotor system,reflexes,incoordination,sensory system,gait,cerebellar and extrapyramidal system examinations.
    iii. Muscle testing which included examination of muscle bulk,tone,power,reflexes,muscle tenderness, identifying specific pattern of muscle involvement and other characteristic signs (eg. polyhill sign in FSHD).

Investigations:

- ❖ All the patients were subjected to routine blood investigations like complete blood count,blood sugar,renal function test,liver function

test,routine urine analysis,thyroid function test,ECG/ECHO study,ophthalmologic evaluation.

- ❖ Other specific investigations included,

1)**Serum CPK measurement:**

Test Procedure

- Blood is drawn from a vein, usually from the arm. The venipuncture area is cleaned with antiseptics. A tourniquet is placed around the upper arm to make the vein prominent. The needle is inserted into the vein, and the blood is allowed to collect in a blood collection tube.

- The blood samples were centrifuged at 3000 RPM for ten minutes immediately after collection, and the serum was removed for analysis of CPK.

- Total enzymatic activity was determined by spectrophotometry and kinetic method.The results are expressed in IU/L.

2) **Nerve conduction study (NCS):**

Nerve conduction studies were done to evaluate the functioning of motor and sensory nerves.

- The muscle electrical signal was recorded and the time from electrical stimulus to muscle contraction (latency),NCV,amplitude determined for both motor and sensory nerves.

3) Electromyography(EMG):

The EMG evaluation to determine the electrical function of individual muscle motor unit potentials at rest and during muscle contraction was done for all patients.

Technique:

- It is performed by inserting a recording needle electrode into the belly of a muscle. The needle tip is the recording electrode and the needle shaft is the reference electrode in a concentric needle.

- Electrical activity from muscle fibers is recorded and amplified to appear on an oscilloscope as a tracing of voltages versus time with accompanying sound.

- spontaneous activity, Motor unit action potentials(MUAPS),Interference pattern were observed and interpreted as normal, myopathic or neurogenic patterns.

- **Interpretation**:

    - Normal-no spontaneous activity, MUAPs with 3-4 phases,amplitude of 0.5 to 2 mV, duration of 5-15ms and a normal interference pattern.

    - Neurogenic:spontaneous activity-present(positive sharp waves, fibrillationpotentials, fasciculations, MUAPs-large amplitude, polyphasic, longer duration, interference pattern-incomplete.

- **Myopathic**- no spontaneous activity(except in myotonic dystrophy, where myotonic discharges are seen), MUAPs-normal to low amplitude, polyphasic,shorter duration, interference pattern-complete with early recruitment.

4)Muscle Biopsy:

- **Technique**: open biopsy procedure was used to obtain muscle specimen in all patients.Under local anesthesia ,a linear piece of muscle tissue of 1.5×0.5 cms size obtained.

- Moderately affected muscles were selected for biopsy.In most of the occasion, Vastus lateralis was sampled and in some patients Tibialis anterior was biopsied.

- Precautions like avoiding severely affected muscles,muscles tested by EMG etc. were followed

- Muscle sample was preserved in saline moistened gauze for transportation to the lab.

- One portion the specimen was flash freezed in isopentane and the cryosectioned specimen used for routine staining (HE/MGT),Enzyme staining(SDH/ATPase).

- 10% formalin fixed paraffin sections were used for routine staining(HE/MAT/PTAH).

Data Analysis:

All the data were tabulated in Microsoft XL sheet,followed by analysis using SPSS software(version 20.0).

RESULTS

A total of 44 patients were included in our study, out of which 32(72.7%) were males and 12(27.3%) were females.

Table - 2

SEX DISTRIBUTION

	Frequency (n)	%
Male	**32**	**73**
Female	**12**	**27**
Total	**44**	**100**

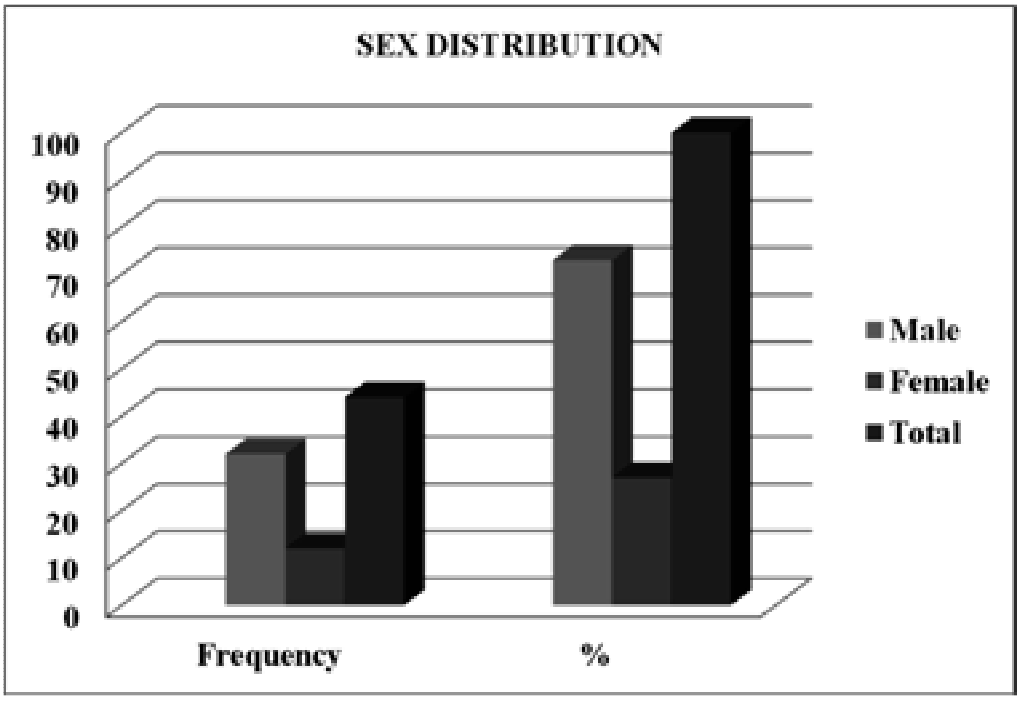

Table - 3

DISTRIBUTION OF VARIOUS HEREDITARY MUSCLE DISORDERS

DIAGNOSIS OF HEREDITARY MUSCLE DISORDERS	FREQUENCY (n)	PERCENT(%)
DMD	2	4.55
BMD	5	11.36
FSHD	5	11.36
LGMD	25	56.81
MYOTONIC DYSTROPHY	3	6.82
DISTAL MYOPATHY	2	4.55
CONGENITAL MYOPATHY	2	4.55
Total	44	100

Among the total of 44 patients,25 were LGMD which accounts 57% of patients.5 patients(11.4%) each in BMD and FSHD were observed.3 patients (6.8%) had myotonic dystrophy.2(4.5%) patients each in DMD,Congenital myopathy and diatal myopathy group were noted in our study.

Table - 4

SEX DISTRIBUTION IN VARIOUS HEREDITARY MUSCLE DISORDERS

DIAGNOSIS OF MUSCLE DISORDERS	SEX				Total	
	Male	%	Female	%		
DMD (n = 2)	2	100	0	0	2	
BMD (n = 5)	5	100	0	0	5	
FSHD (n = 5)	4	80	1	20	5	p<0.091
LGMD (n = 25)	16	64	9	36	25	
MYOTONIC DYSTROPHY (n = 3)	3	100	0	0	3	
DISTAL MYOPATHY (n = 2)	0	0	2	100	2	
CONGENITAL MYOPATHY (n = 2)	2	100	0	0	2	

Among 25 LGMD patients,16 (64%)were males and 9(36%) are females. Out of 5 patients with BMD, all 5(100%) were males. Among 5 FSHD, 4(80%) were males and 1(20%) was female. 3 patients had Myotonic dystrophy. All 3(100%) were males. Total of 2 had Distal Myopathy and all 2(100%) were females. 2 had Congenital Myopathy and all 2(100%) were males. All 2(100%) patients with DMD were males.

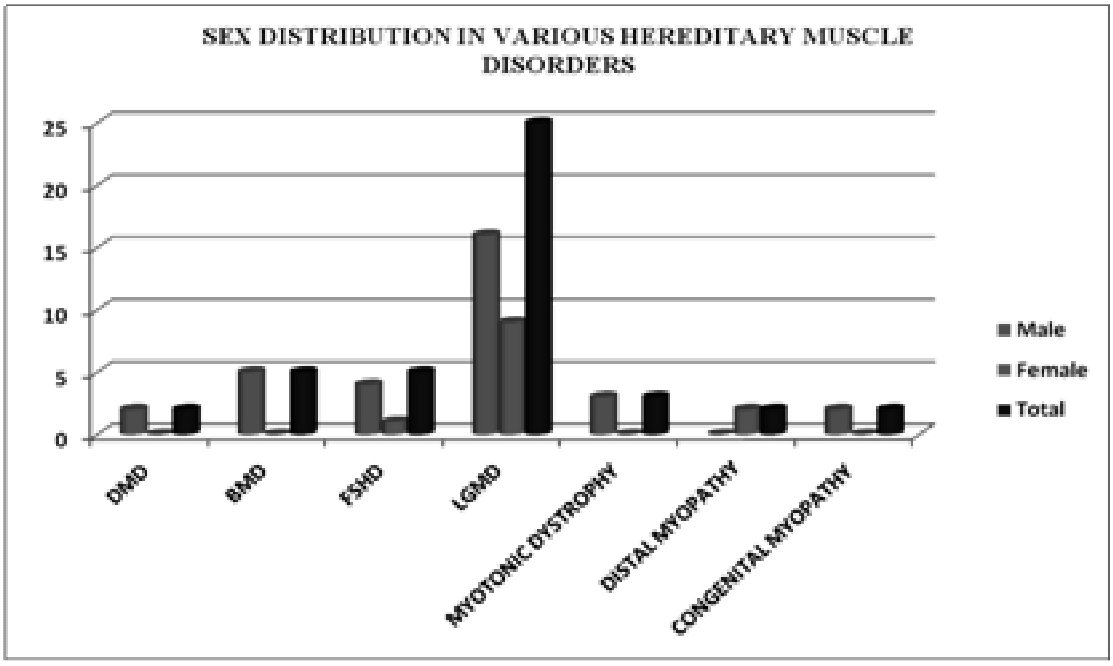

Figure - 1

Biceps hump in a patient with LGMD

Table - 5

AGE DISTRIBUTION OF PATIENTS WITH HEREDITARY MUSCLE DISORDERS

DIAGNOSIS OF MUSCLE DISORDERS	Age Groups (Yrs)					Total	
	1 – 10	11 – 20	21 – 30	31 – 40	41 – 50		
DMD (n = 2)	2	0	0	0	0	2	p<0.083
BMD (n = 5)	3	1	0	1	0	5	
FSHD (n = 5)	1	2	0	1	1	5	
LGMD (n = 25)	3	11	6	4	1	25	
MYOTONIC DYSTROPHY (n = 3)	0	2	0	1	0	3	
DISTAL MYOPATHY (n = 2)	0	0	2	0	0	2	
CONGENITAL MYOPATHY (n = 2)	0	2	0	0	0	2	
Total	9	18	8	7	2	44	

Among 25 patients with LGMD, 11(44%) belong to the age group of 11-20yrs, 6(24%) to 21-30yrs, 4(16%) to 31-40yrs, 3(12%) to 1-10yrs and 1(4%) to 41-50. Out of 5 affected with FSHD, 2(40%) belong to the age group of 11-20yrs, 1(20%) to 1-10yrs, 1(20%) to 31-40yrs, 1(20%) to 41-50yrs. In a total of BMD patients, 3(40%) belong to age group of 1-10yrs , 1(20%) in the age group of 11-20yrs and 1(20%) in the age group of 31-40 yrs. out of 3with Myotonic dystrophy 2(66.67%) belong to age group of 11-20yrs and 1(33.33%) to 31-40yrs. All 2 (100%) with Distal Myopathy belong to the age group of 21-30yrs. All 2(100%) with Congenital myopathy belong to the age group of 11-20yrss. All 2(100%) of DMD patients belong to age group of 1-10yrs. The mean age of the

patients with muscle disorders was 24.38 yrs with Standard deviation (SD) 11.82 yrs.

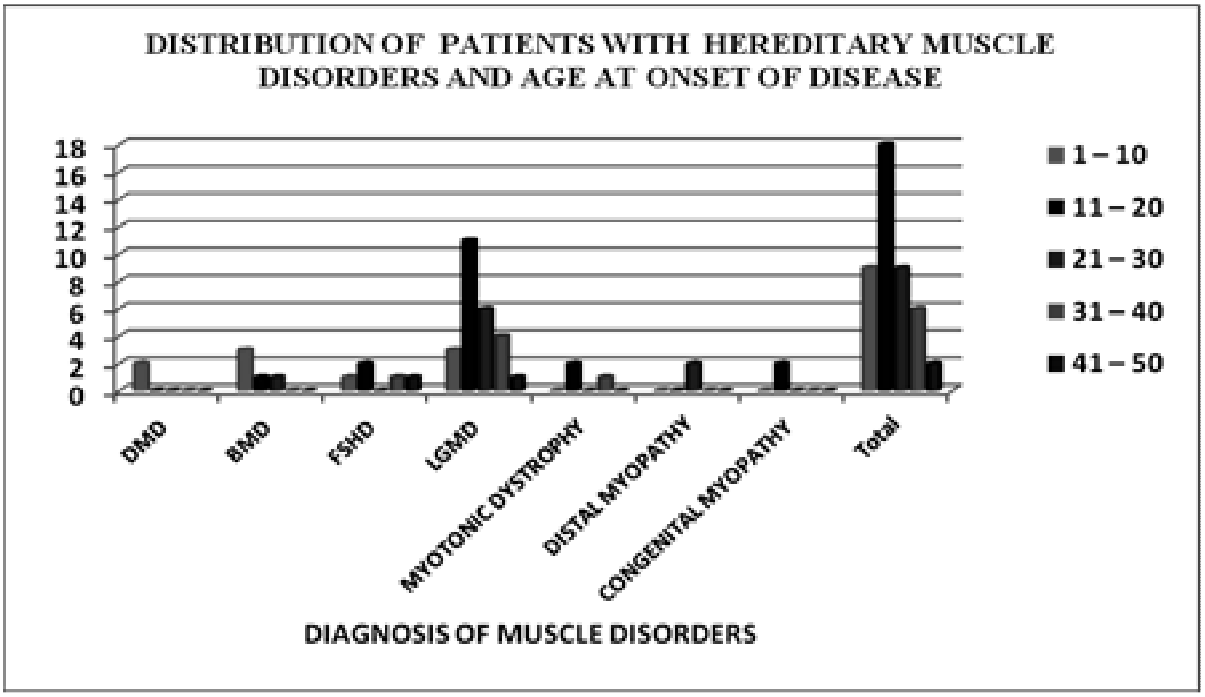

Table – 6
DISTRIBUTION OF AGE AT ONSET AMONG HEREDITARY MUSCLE DISORDERS

DIAGNOSIS OF MUSCLE DISORDERS	Grouping of Age at onset of Disease					Total	
	1 – 10	11 – 20	21 – 30	31 – 40	41 – 50		
DMD (n = 2)	2	0	0	0	0	2	
BMD (n = 5)	3	1	1	0	0	5	
FSHD (n = 5)	1	2	0	1	1	5	
LGMD (n = 25)	3	11	6	4	1	25	p <0.083
MYOTONIC DYSTROPHY (n = 3)	0	2	0	1	0	3	
DISTAL MYOPATHY (n = 2)	0	0	2	0	0	2	
CONGENITAL MYOPATHY (n = 2)	0	2	0	0	0	2	
Total	9	18	9	6	2	44	

In a total of 25 patients with LGMD 11(44%) had disease onset between 11-20yrs, 6(24%) in 21-30yrs, 4(16%) in 31-40yrs, 3(12%) in 1-10yrs and 1(4%) in 41-50yrs. Out of 5 affected with FSHD, 2(40%) had disease onset between 11-20yrs, 1(20%) in 1-10yrs,1(20%) in 31-40yrs and 1(20%) in 41-50yrs. Out of 5 patients with BMD, 3(40%) had disease onset in the age group of 1-10yrs , 1(20%) in 11-20yrs and 1(20%) in 21-30 yrs.Out of 3 with Myotonic dystrophy,2(66.67%) had disease onset in the age group of 11-20yrs and 1(33.33%) in 31-40yrs.All 2 (100%)patients with Distal Myopathy had disease at onset in the age group of 21-30yrs. All 2 (100%) with Congenital myopathy had disease at onset in the age group of 11-20yrs. All 2(100%) patients with DMD had disease of onset in the age group of 1-10yrs. The mean age of onset of the disease in patients with muscle disorders was 19.31 yrs with Standard deviation (SD) 11.08 yrs.

Table – 7
DISTRIBUTION OF PATIENTS WITH HEREDITARY MUSCLE DISORDERS AND DURATION OF THE DISEASE

DIAGNOSIS OF MUSCLE DISORDERS	Duration of disease (Yrs)				Total	
	1 – 5	6 – 10	11 – 15	16 – 20		
DMD (n = 2)	0	2	0	0	2	p<0.574
BMD (n = 5)	3	1	1	0	5	
FSHD (n = 5)	2	1	2	0	5	
LGMD (n = 25)	16	8	1	0	25	
MYOTONIC DYSTROPHY (n = 3)	2	1	0	0	3	
DISTAL MYOPATHY (n = 2)	2	0	0	0	2	
CONGENITAL MYOPATHY (n = 2)	2	0	0	0	2	
Total	27	13	4	0	44	

Among 25 patients with LGMD, 16(64%)had a duration of 1-5yrs, 8(32%) of 6-10yrs, 1(4%) of 11-15yrs. Out of 5 affected with FSHD, 2(40%) were suffering for a period of 1-5yrs, 1(20%) for 6-10yrs and 2(40%) for 11-15yrs. Among 5 patients with BMD, 3(40%) were suffering for a period of 1-5yrs , 1(20%) for 6-10yrs and 1(20%) for 11-15yrs. Out of 3 patients with Myotonic dystrophy, 2(66.67%) had a duration of 1-5yrs and 1(33.33%) had duration of 6-10yrs. All 2(100%) patients with Distal myopathy were suffering for a period of 1-5yrs. All 2(100%) affected with Congenital myopathy were suffering for a period of 1-5yrs. The 2(100%) DMD affected person had been suffering from the disease for 6-10yrs. The mean duration of the disease in patients with muscle disorders was 5.3 yrs with Standard deviation (SD) 3.76 yrs.

Table – 8

INHERITANCE PATTERN IN VARIOUS HEREDITARY MUSCLE DISORDERS

DIAGNOSIS OF MUSCLE DISORDERS	FAMILY HISTORY				Total	
	Autosomal Recessive	Autosomal Dominant	X-linked recessive	Not clear		
DMD (n = 2)	0	0	2	0	2	
BMD (n = 5)	0	0	4	1	5	
FSHD (n = 5)	0	0	0	5	5	
LGMD (n = 25)	7	0	0	18	25	
MYOTONIC DYSTROPHY (n = 3)	0	2	0	1	3	p<0.001
DISTAL MYOPATHY (n = 2)	0	1	0	1	2	
CONGENITAL MYOPATHY (n = 2)	1	1	0	0	2	
Total	8	4	6	26	44	

Among 25 patients with LGMD, 18(72%) had no or unclear family history and 7(28%) had autosomal recessive inheritance. None of the 5(100%) patients with FSHD, had family history. Among the 5 with BMD, 4(80%) have XR pattern of inheritance and 1(20%) had no family history. Out of 3 with Myotonic dystrophy, 2(66.7%) had autosomal dominant type of inheritance and 1(33.33%) had no family history.

Among 2 with Distal myopathy, 1(50%) had autosominal dominant type of inheritance and 1(50%) had no family history. Out of 2 with congenital myopathy 1(50%) had autosomal recessive type of inheritance and 1(50%) had autosomal dominant type of inheritance. All 2(100%) with DMD had XR type of inheritance. The distribution of the subjects with muscle disorders and type of their inheritance was found to be statistically significant (p<0.001).

Table - 9

DISTRIBUTION OF THE SUBJECTS WITH DIAGNOSIS OF HEREDITARY MUSCLE DISORDERS AND SYMMETRICITY OF WEAKNESS

DIAGNOSIS OF MUSCLE DISORDERS	WEAKNESS		Total	
	Symmetrical(%)	Asymmetrical(%)		
DMD (n = 2)	2	0	2	
BMD (n = 5)	5	0	5	
FSHD (n = 5)	2	3	5	
LGMD (n = 25)	24	1	25	p<0.007
MYOTONIC DYSTROPHY (n = 3)	3	0	3	
DISTAL MYOPATHY (n = 2)	2	0	2	
CONGENITAL MYOPATHY (n = 2)	2	0	2	
Total	40	4	44	

In a total of 25 patients with LGMD, 24(96%) had symmetrical weakness and 1(4%) had asymmetrical weakness. Out of 5 patients with FSHD, 2(40%) had symmetrical weakness and 3(60%) had asymmetrical weakness. All 5 patients with BMD had symmetrical weakness. All 3(100%) patients with Myotonic dystrophy had symmetrical weakness. All 2(100%) patients with DMD had symmetrical weakness. All 2(100%) patients with Distal Myopathy had symmetrical weakness. All 2(100%) suffering from Congenital myopathy had symmetrical weakness. Distribution of subjects with diagnosis and pattern of weakness was found to be statistically significant($p<0.007$).

Table - 10
DISTRIBUTION OF THE WEAKNESS AMONG VARIOUS HEREDITARY MUSCLE DISORDERS

DIAGNOSIS OF MUSCLE DISORDERS	DISTRIBUTION OF WEAKNESS			Total	
	PROXIMAL	DISTAL	BOTH		
DMD (n = 2)	1	0	1	2	
BMD (n = 5)	4	0	1	5	
FSHD (n = 5)	3	0	2	5	p<0.001
LGMD (n = 25)	12	0	13	25	
MYOTONIC DYSTROPHY (n = 3)	1	1	1	3	
DISTAL MYOPATHY (n = 2)	0	2	2	2	
CONGENITAL MYOPATHY (n = 2)	2	0	0	2	
Total	23	3	18	44	

Among 25 patients with LGMD, 12(48%) had proximal weakness and 13(52%) had both proximal and distal weakness. Among 5 with BMD, 4(80%) had proximal and 1(20%) had proximal and distal weakness. Among 5 with FSHD, 3(60%) had proximal weakness and 2(40%) had both proximal and distal weakness. Out of 3 with Myotonic dystrophy, 1(33.3%) had proximal weakness, 1(33.3%) had distal weakness and 1(33.3%) had both. Among 2 with DMD, 1(50%) had proximal weakness and 1(50%) had both. All 2(100%) patients with distal myopathy had distal weakness. 2(100%) patients with Congenital myopathy had proximal weakness. It was found that the distribution of weakness among various hereditary muscle disorders and the part of the body affected was found to be statistically significant ($p<0.001$).

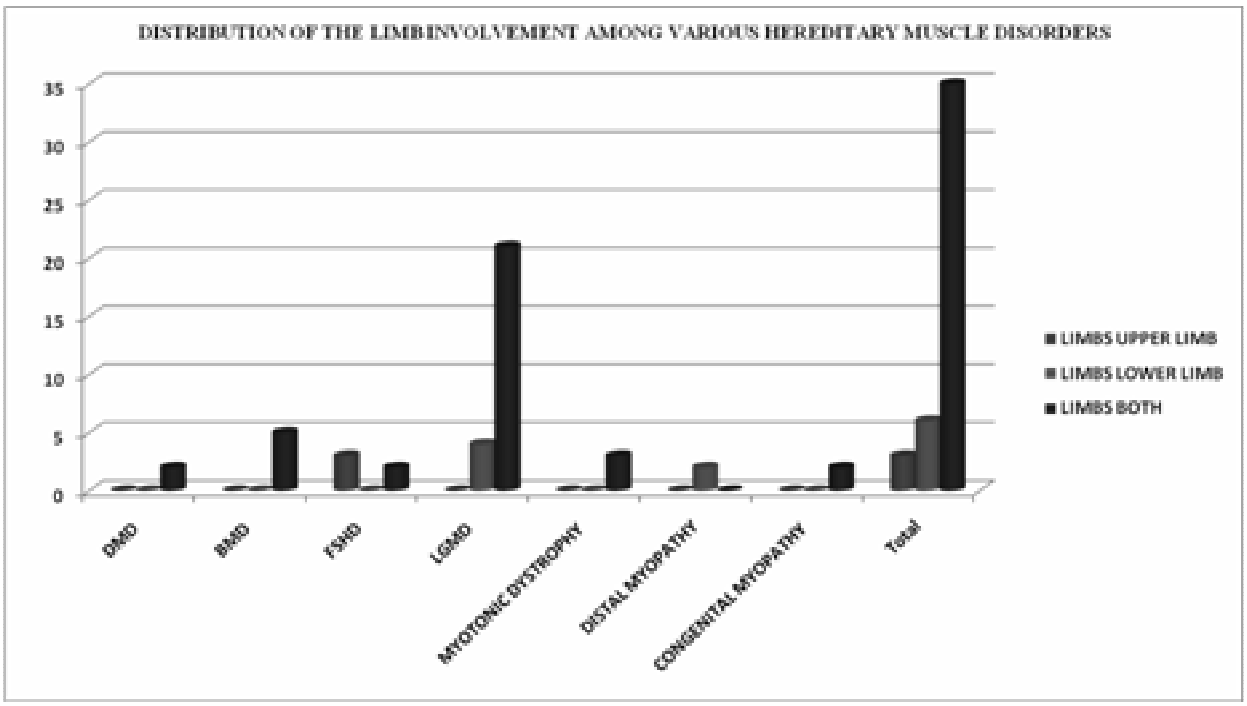

Table - 11

DISTRIBUTION OF THE LIMB INVOLVEMENT AMONG VARIOUS HEREDITARY MUSCLE DISORDERS

DIAGNOSIS OF MUSCLE DISORDERS	LIMBS			Total	
	UPPER LIMB	LOWER LIMB	BOTH		
DMD (n = 2)	0	0	2	2	
BMD (n = 5)	0	0	5	5	
FSHD (n = 5)	3	0	2	5	p<0.001
LGMD (n = 25)	0	4	21	25	
MYOTONIC DYSTROPHY (n = 3)	0	0	3	3	
DISTAL MYOPATHY (n = 2)	0	2	0	2	
CONGENITAL MYOPATHY (n = 2)	0	0	2	2	
Total	3	6	35	44	

Among 25 patients with LGMD, 21(84%) had both upper and lower limb involved and 4(16%) had only lower limb involved. Out of 5 with FSHD, 3(60%) had only upper limb involvement and 2(40%) had both upper and lower limb involved. All 5(100%) with BMD had both upper and lower limb involvement. All 3(100%) with Myotonic dystrophy had both upper and lower limb involvement. All 2 (100%) patients with DMD had both upper and lower limb involvement. All 2(100%) with Distal myopathy had only involvement of lower limbs. All 2(100%) with Congenital myopathy had both upper and lower limb involved. The distribution of limb involvement among various hereditary muscle disorders was found to be statistically significant ($p<0.001$).

Figure – 2
Scapular winging in one of our patient with FSHD
(Angel wing appearance)

Table - 12
PATTERN OF INVOLVEMENT IN HEREDITARY MUSCLE DISORDERS

CLINICAL DIAGNOSIS	PATTERN OF INVOLVEMENT						Total
	Pattern 1	Pattern 2	Pattern 3	Pattern 4	Pattern 5	Pattern 6	
DMD	2(100%)	0	0	0	0	0	2
BMD	5(100%)	0	0	0	0	0	5
FSHD	4(80%)	0	1(20%)	0	0	0	5
LGMD	25(100%)	0	0	0	0	0	25
Myotonic-dystrophy	2(66.7%)	1(33.3%)	0	0	0	0	3
Congenital-myopathy	2(100%)	0	0	0	0	0	2
Distal-myopathy	0	2(100%)	0	0	0	0	2
Total	40	3	1	0	0	0	44

Pattern-1 - proximal limb-girdle, Pattern-2 - distal weakness, Pattern-3 - proximal arm/distal leg weakness, Pattern-4 - distal arm/proximal leg weakness, Pattern-5 -ptosis with or without ophthalmoplegia, pattern-6 - prominent neck extensor weakness.

Proximal limb-girdle pattern (90.9%) was the most common pattern of weakness in our study,which was found in all(100%) of patients with DMD, BMD,LGMD,Congenital myopathy and in 4(80 %) of patients with FSHD.It was also seen in 2(66.7%) of patients with myotonic dystrophy.The next common pattern was distal pattern (6.8%) which was found in all 2(100%) of patients with distal myopathy and in 1(33.3%) patient with myotonic myopathy.The third pattern, proximal arm/distal leg pattern (2.3%)was found in 1(20%) of patients with FSHD. No other pattern of weakness was found in our study.

Table - 13
SPECIFIC CLINICAL SIGNS

Clinical signs	DMD	BMD	LGMD	FSHD	Myotonic dystrophy	Congenital myopathy	Distal myopathy
Calf Hypertrophy	2 (100%)	4 (80%)	5 (20%)	0	0	0	0
Gowers sign	2 (100%)	2 (40%)	7 (28%)	0	0	0	0
Scapular winging	0	0	5 (20%)	5 (100%)	0	0	0
Polyhill sign	0	0	0	5 (100%)	0	0	0
Calf atrophy	0	0	3 (12%)	0	0	0	1 (50%)
Diamond quadriceps	0	0	4 (16%)	0	0	0	0
Hip abduction sign	0	0	8 (32%)	0	0	0	0
Biceps lump	0	0	4 (16%)	0	0	0	0
Valley sign	1 (50%)	1 (20%)	1 (4%)	0	0	0	0
Contractures	1 (50%)	1 (20%)	4 (16%)	0	0	0	0
Hatchet facies	0	0	0	0	2 (66.7%)	0	0
Myotonia	0	0	0	0	3 (100%)	0	0

Specific clinical findings found among various hereditary muscle disorders in our study are shown in the table 11.All 5(100%) 0f patients with FSHD had polyhill sign and scapular winging.All 2(100%) of patients with DMD had gower's sign and calf hypertrophy.All 3(100%) patients with myotonic dystrophy had percussion or grip myotonia.Biceps

hump(16%),Diamond quadriceps(16%),Hip abduction sign(32%),calf atrophy(12%) were the specific signs noted in our LGMD patients.

Table – 14

DISTRIBUTION OF SUBJECTS WITH DIAGNOSIS OF HEREDITARY MUSCLE DISORDERS AND SERUM CREATINE KINASE VALUE

DIAGNOSIS OF MUSCLE DISORDERS	VALUE OF SERUM CREATINE KINASE							Total	
	<250	251 – 1000	1001 – 2000	2001 – 3000	3001 - 4000	5001 - 6000	8001 - 9000		
DMD (n = 2)	0	0	1	0	0	1	0	2	
BMD (n = 5)	0	0	1	1	1	2	0	5	
FSHD (n = 5)	2	3	0	0	0	0	0	5	
LGMD (n = 25)	0	12	9	0	3	0	1	25	p<0.031
MYOTONIC DYSTROPHY (n = 3)	0	1	2	0	0	0	0	3	
DISTAL MYOPATHY (n = 2)	0	2	0	0	0	0	0	2	
CONGENITAL MYOPATHY (n = 2)	0	2	0	0	0	0	0	2	
Total	2	20	13	1	4	3	1	44	

Among 25 patients with LGMD 12(48%) had serum creatinine kinase(CK) level between 251-1000,9(36%) between 1001-2000 and 3(12%) have between 3001 – 4000.Out of 5 with BMD 2(40%) had CPK between 5001 – 6000,1(20%) had between 1001-2000 and 1(20%) between 2001-3000 and 1(20%) had between 3001-4000. Among 5 with FSHD 2(40%) have CK level < 250 and 3(60%) have between 251 to 1000. Out of 3 with Myotonic dystrophy, 2(66.67%) have CK level between1001- 2000 and 1(33.33%) had between 251-1000. All 2(100%) with distal myopathy have CK level between 251-1000. All 2 (100%)with Congenital myopathy had CK level between 251-1000. Out of 2 with DMD, 1(50%) had CK level between 1001-2000 and 1(50%) had between 5001-6000.The differences in the CPK level among patients with muscle disorders was found to be statistically significant(p< 0.031).

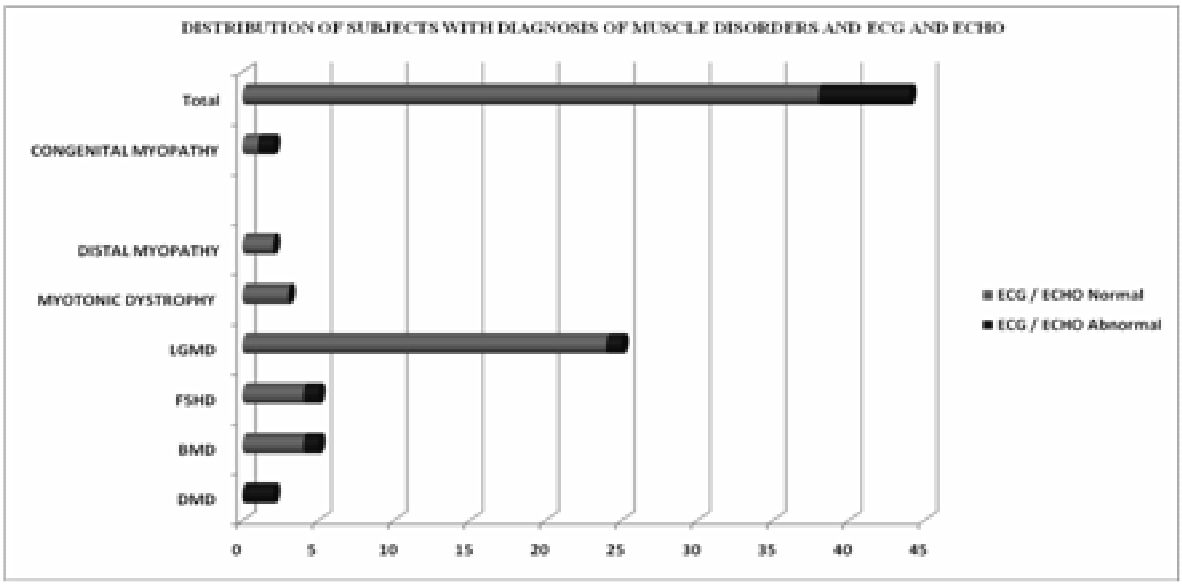

Table - 15

DISTRIBUTION OF SUBJECTS WITH DIAGNOSIS OF HEREDITARY MUSCLE DISORDERS AND ECG AND ECHO

DIAGNOSIS OF MUSCLE DISORDERS	ECG / ECHO		Total	
	Normal	Abnormal		
DMD (n = 2)	0	2	2	
BMD (n = 5)	4	1	5	
FSHD (n = 5)	4	1	5	
LGMD (n = 25)	24	1	25	p<0.006
MYOTONIC DYSTROPHY (n = 3)	3	0	3	
DISTAL MYOPATHY (n = 2)	2	0	2	
CONGENITAL MYOPATHY (n = 2)	1	1	2	
Total	38	6	44	

Out of 25 patients with LGMD, 24(96%) had normal cardiac status, while 1(4%) had abnormal cardiac status. Among 5 with FSHD, 4(80%) had normal cardiac status and 1(20%) had abnormality. Among 5 with BMD, 4(80%) had normal cardiac status and (20%) had abnormality. All 3(100%) with Myotonic dystrophy had normal cardiac status.All 2(100%) with DMD had normal cardiac status. All 2(100%) with Distal myopathy had normal status. Among 2 with Congenital myopathy,1(50%) had normal and 1(50%) had abnormal cardiac status.The difference was found to be statistically significant($p<0.006$).

Table – 16
DISTRIBUTION OF SUBJECTS WITH DIAGNOSIS OF MUSCLE DISORDERS AND EMG

DIAGNOSIS OF MUSCLE DISORDERS	EMG		Total	
	MYOPATHIC	MYOTONIC		
DMD (n = 2)	2	0	2	
BMD (n = 5)	5	0	5	
FSHD (n = 5)	5	0	5	p<0.001
LGMD (n = 25)	25	0	25	
MYOTOINIC DYSTROPHY (n = 3)	0	3	3	
DISTAL MYOPATHY (n = 2)	2	0	2	
CONGENITAL MYOPATHY (n = 2)	2	0	2	
Total	41	3	44	

All 25(100%) with LGMD had myopathic EMG pattern. All 5(100%) with FSHD had myopathic pattern. All 5(100%) with BMD had myopathic pattern. All 3 (100%)with Myotonic dystrophy had myotonic picture. All 2 (100%)with DMD had myopathic picture in EMG. All 2(100%) with Distal myopathy had myopathic picture. All 2(100%) with Congenital myopathy had myopathic picture.The differences was found to be statistically significant($p<0.001$).

Table – 17

DISTRIBUTION OF SUBJECTS WITH DIAGNOSIS OF MUSCLE DISORDERS AND MUSCLE BIOPSY

DIAGNOSIS OF MUSCLE DISORDERS	MUSCLE BIOPSY		Total	
	MD	NO DYSTROPHY		
DMD (n = 2)	2	0	2	
BMD (n = 5)	5	0	5	
FSHD (n = 5)	5	0	5	
LGMD (n = 25)	25	0	25	p<0.009
MYOTONIC DYSTROPHY (n = 3)	2	1	3	
DISTAL MYOPATHY (n = 2)	2	0	2	
CONGENITAL MYOPATHY (n = 2)	1	1	2	
Total	42	2	44	

MD-Muscular dystrophy

All 25(100%) patients with LGMD showed muscle dystrophy in muscle biopsy. All 5(100%) with FSHD showed muscle dystrophy. All 5(100%) with BMD showed muscle dystrophy. Out of 3 with Myotonic dystrophy, 2(66.67%) showed muscle dystrophy and 1(33.33%) showed no muscle dystrophy. Out of 2 with congenital myopathy, 1(50%) showed muscle dystrophy and the other(50%)had specific feature(Nemaline rods)

but without dystrophy. All 2(100%) with DMD showed muscle dystrophic pattern. All the 2 (100%)with distal myopathy showed muscle dystrophy and the differences was statistically significant($p<0.009$).

Table 18

CORRELATION BETWEEN THE CLINICAL DIAGNOSIS OF HEREDITARY MUSCLE DISORDERS AND ELEVATED SERUM CREATINE KINASE VALUE

		ELEVATED SERUM CREATINE KINASE VALUE	CLINICAL DIAGNOSIS
ELEVATED SERUM CREATINE KINASEVALUE	Pearson Correlation	1	.413**
	Sig. (2-tailed)		.005
	N	44	44
CLINICAL DIAGNOSIS	Pearson Correlation	.413**	1
	Sig. (2-tailed)	.005	
	N	44	44

****. Correlation is significant at the 0.01 level (2-tailed).**

A high degree of correlation was found between the clinical diagnosis of hereditary muscle disorders and elevated serum creatine kinase which was statistically significant with a p value of <0.005.

Table 19

CORRELATION BETWEEN THE CLINICAL DIAGNOSIS OF HEREDITARY MUSCLE DISORDERS AND MYOPATHIC EMG

			MYOPATHIC EMG	CLINICAL DIAGNOSIS
Spearman's rho	MYOPATHIC EMG	Correlation Coefficient	1.000	.487**
		Sig. (2-tailed)	.	.001
		N	44	44
	CLINICAL DIAGNOSIS	Correlation Coefficient	.487**	1.000
		Sig. (2-tailed)	.001	.
		N	44	44

****. Correlation is significant at the 0.01 level (2-tailed).**

A high degree of correlation was found between the clinical diagnosis of hereditary muscle disorders and myopathic EMG which was statistically significant with a p value of <0.001.

Table 20

CORRELATION BETWEEN THE CLINICAL DIAGNOSIS OF HEREDITARY MUSCLE DISORDERS AND MYOPATHIC PATTERN OF MUSCLE BIOPSY

			MYOPATHIC PATTERN OF MUSCLE BIOPSY	CLINICAL DIAGNOSIS
Spearman's rho	MYOPATHIC PATTERN OF MUSCLE BIOPSY	Correlation Coefficient	1.000	.357*
		Sig. (2-tailed)	.	.017
		N	44	44
	CLINICAL DIAGNOSIS	Correlation Coefficient	.357*	1.000
		Sig. (2-tailed)	.017	.
		N	44	44

*. Correlation is significant at the 0.05 level (2-tailed).

A high degree of correlation was found between the clinical diagnosis of hereditary muscle disorders and myopathic pattern in muscle biopsy which was statistically significant with a p value of <0.005.

DISCUSSION

Hereditary muscle disorders are more common than acquired myopathies.clinical suspicion,correct approach and appropriate investigations will lead us to an accurate diagnosis.Demographic and clinical spectrum of hereditary muscle disorders with its correlation to laboratory parameters are discussed in the following section.

In our study with a total of 44 patients ,32(72.7%) were males and 12(26.3%) were females.In LGMD out of 25 patients,16(64%) were males and 9(36%) were females,whereas in a study by **Meena et al**[18] it was 54% and 46% for males and females respectively. All 2(100%) patients with congenital myopathy were females.

In a total of 44 patients with hereditary muscle disorders,40(91%) were muscular dystrophies.LGMD is the most common hereditary muscle disorders in our study(57%) and DMD is found in only 5%,which is in contrast to a study by **Das et al**[19] where both DMD(30%) and LGMD(29.2%) were equally prevalent.This gross difference in prevalence in our study could be due to the fact that most of the DMD patients possibly were evaluated and treated by paediatric neurologist whereas our centre is an adult referral hospital and so only ,less number of patients were referred here for neurological consultation. According to

another Indian study(**Khadhilkar S V et al**) LGMD formed the most common hereditary muscle disorder, which is consistent with our study.[20]

The age distribution in our patients showed that 20% of the patients were in the age group of less than 15 years which is in line with a study by **Buchthal F et al**,[21] in which 25% of the myopathic patients were in that age group.Majority of our patients were young(2nd decade).No patients with hereditary muscle disorders are found beyond 5th decade in our study.Earliest age at onset in our study was 2 years(DMD) and late age at onset was 50 years(FSHD).All 2(100%) patients with congenital myopathy had age at onset in 3rd decade.This shows that our patients with congenital myopathy could be the milder adult onset variants.[22]All 2 (100%) patients with distal myopathy had early age onset (2nd decade),one of the patient had autosomal dominant mode of inheritance(Laing syndrome).The other patient had no clear family history,without neck weakness and the biopsy showed fibre necrosis without rimmed vacuoles and so she could be a case of miyoshi myopathy.This shows that the distal myopathy(Laing or Miyoshi) are not uncommon in our population.

Among all patients with muscular dystrophies(40), only 3(7.5%) were myotonic dystrophy which correlates with another Indian study(8%)

by **Gourie devi et al**.[23]FSHD constitutes 12.5% of patients with muscular dystrophies,which is in contrast to other Indian studies where only 2.3% and 1.3% were seen by **Srinivas et al.**[24] and **Das et al** respectively.congenital myopathy and distal myopathy were diagnosed in 2(4.5%) patients each, equal to the incidence of DMD(4.5%) which is consistent with the incidence from a study by **Nonaka I et al**.[25]

Among 44 patients only 4(9.1%) patients had asymmetric weakness.As comparable to many previous studies, asymmetric weakness was more common in FSHD patients(6.8%).In our study , asymmetric muscle weakness was also noted in a patient with LGMD(2.3%) which was also observed in previous study by Khadilkar S V et al(42%).[26]

Most of our patients with positive family history had autosomal recessive mode of inheritance and this could be due to the commonly practiced custom of consanguineous marriage in our population.Next common mode of inheritance was X-linked recessive followed by autosomal dominant pattern. Among LGMD 28% of patients had AR pattern and no patients had AD pattern of inheritance,which correlates well with a previous Indian study by Khadhilkar et al.

Weakness involving both upper and lower limbs were commonly seen in our patients(79.5%) which is consistent with many previous

studies.[27]This could possibly due to the fact that most of our patients seek medical advice only late in the illness.Only upper limb weakness without involving lower limbs were noted in 3(60%) patients with FSHD which is parallel to a study by **Pradhan et al**.[28]Weakness of only lower limbs without upper limb weakness were observed in all 2(100%)patients with distal myopathy and in 16% of patients with LGMD.

Pattern of involvement is important in the clinical diagnosis of hereditary muscle disorders,because each of these disorders have a distinct pattern in most of the occasions.Most of our patients(88.6%) had proximal limb-girdle pattern of muscle weakness and patients with hereditary muscle disorders like DMD (100%),BMD(100%),LGMD(100%),congenital myopathy (100%) were fitting well in this group. This is consistent with many previous studies (**Barohn RJ et al**)[4].Next common pattern seen was the distal pattern, with both the patients of distal myopathy (100%) and myotonic dystrophy(33.3%) were observed. The third pattern with proximal arm/distal leg weakness was seen in only one patient(FSHD).

Many specific clinical signs were described that helps to diagnose hereditary muscle disorders with certainty.Calf hypertrophy was observed in DMD(100%),BMD(80%) and in some of the LGMD patients(20%).In

contrast to our study,53.8% of patients with LGMD(Sarcoglycanopathies) had calf hypertrophy in a study by Meena et al,.[29]Gowers sign was seen in DMD(100%),BMD(40%) and in 28% of patients with LGMD.This sign along with calf hypertrophy in young boys are diagnostic of DMD(**Mansur et al**)[30].Contractures in patients with muscular dystrophy is well described in literature which was also noted in our patients.Contractures were seen in DMD(50%),BMD(20%) and in LGMD(16%) which correlates with a study by Mansur et al.

All 5(100%) patients with FSHD had polyhill sign which is due to a differential wasting in certain muscles with relative preservation of muscle bulk around shoulder girdle.This is specifically seen in patients with FSHD(Pradhan et al).[28]Winging of scapula(Angel wing appearance) was also seen in all 5(100%) of patients with FSHD, but this was also noted in some LGMD patients.Atrophy of calf muscles(12%),Biceps lump(due to differential wasting in biceps)16% and Diamond quadriceps(16%) were also noted in our patients with LGMD,which has been described in patients with LGMD(dysferlinopathy) by **Pradhan et al,**.[31,32]

Hip abductor sign with splaying of legs while getting up from squatting ,which occurs due the profound weakness of hip adductors with

preserved hip abductors is well documented to occur in patients with LGMD like sarcoglycanopathy(Khadhilkar et al).[33]This sign was seen in 8(32%) patients with LGMD in our study.Hip abductor sign is helpful in differentiating LGMD from DMD/BMD,since in the later hip abductors,quadriceps and iliopsoas are involved earlier with severe degree of weakness as compared to hip adductor/hamstrings involvement in LGMD.The specific signs that are described in literature were also noted in our study,but only in a lesser number of patients.

Valley sign(due to the prominent wasting in posterior axillary muscles with relatively preserved deltoid and infraspinatus) described by Pradhan et al,was observed in 1(50%)patient with DMD,1 with BMD(20%) and1with LGMD(4%) in our study.[34]

CK elevation was found in all patients in our study, but the degree of elevation differs among various hereditary muscle disorders(Wong E T et al).[5]It was maximal(>25 times normal)in patients with DMD(50%),BMD(40%) and in LGMD(4%).All these patients had similar phenotype with severe degree of weakness.Mild to moderate elevations(2-25 times normal) was found in most of our patients with LGMD,congenital myopathy and distal myopathy.Minimal elevation was found in FSHD patients as described in literature.[35]

In a previous study by Mansur et al,72% of BMD patients had cardiac involvement which was not found in our study where only 20% had abnormal ECG/ECHO findings.Whereas all 2(100%) DMD patients,1(20%) FSHD,1(4%) of LGMD and1(50%) of congenital myopathy had cardiac involvement.

High degree of correlation between clinical diagnosis of hereditary muscle disorders and myopathic EMG was found.Myopathic pattern was observed in all patients of Muscular dystrophy,congenital myopathy and distal myopathy. All 3(100%) myotonic dystrophy patients showed spontaneous activity(myotonic discharges) in EMG study.This is consistent with other previous studies(**Garima Shukla et al ,Black JT et al. ,Peter K et al. ,Buchthal et al.**).[36,37,38,19]

Muscle biopsy study in our patients showed that,all patients with muscular dystrophy(100%),1(50%) patient with congenital myopathy and in 2(66.7%) patients with myotonic dystrophy had myopathic pattern.1(50%) patient with congenital myopathy had specific changes of internal structure in muscle fibres(Nemaline rods).[39]Clinical diagnosis of hereditary muscle disorders and concordant myopathic pattern in muscle biopsy study was found in more than 90% of our patients as comparable to many previous studies(Buchthal et al. ,Peter K et al..Schwartz et al,).[19,38,40]

CONCLUSION

In conclusion, the following observations were made from our study,

- Hereditary muscle disorders are common among males than in females.

- Most of the patients with hereditary muscle disorders were in the age group of 10 to 20 years(2^{nd} decade).

- Earliest age of onset in our study was 2 years (DMD).

- No patients with hereditary muscle disorders were found beyond 5^{th} decade in our study.

- Most common hereditary muscle disorders was LGMD(57%) followed by FSHD(11.4%) and BMD(11.4%).

- Most common pattern of involvement was proximal limb girdle pattern with all DMD, BMD, LGMD, Congenital myopathy patients in that group.

- Polyhill sign and scapular winging were seen in all our patients with FSHD, which is a characteristic finding in this disease. Specific clinical signs were less commonly noted in our patients with LGMD.

- Serum CK elevation is maximum (>25 times normal) in DMD, BMD, LGMD(AR inheritance) and minimum(1-2 times normal) in FSHD and the CK elevation correlates well with the

clinical phenotype among various hereditary muscle disorders in our population. A strong correlation between elevated serum CK and clinical diagnosis of hereditary muscle disorders was noted in our study.

- High degree of concordance of clinical diagnosis of hereditary muscle disorders with EMG was observed in our study.

- High degree of concordance of clinical diagnosis of hereditary muscle disorders with muscle biopsy was observed in our study.

Hence, a structured clinical approach focusing on pattern of muscle involvement and on specific clinical signs along with investigations like serum CPK,EMG and Muscle biopsy,it is possible to make an accurate early diagnosis in hereditary muscle disorders,prognosticate and manage them appropriately to improve the quality of life in these patients.

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ABBREVIATIONS

BMD	:	Becker's muscular dystrophy
CK	:	Creatine Kinase
DMD	:	Duchene muscular dystrophy
EMG	:	Electromyography
FSHD	:	Facioscapulohumeral muscular dystrophy
LGMD	:	Limb Girdle muscular dystrophy
MD	:	Muscular dystrophy
MUAP	:	Motor unit action potenial

MASTER CHART

Sl.No.	Name	Sex	Age	OP/IP No.	HISTORY								
					Age at onset (Yrs)	Mode of onset	Duration of Illness (Yrs)	Progression	H/o Fatiguability	H/o Diurnal Variation	H/o constitutional symptoms	H/o Muscle Pain	H/o Chronic drug usage/ Exposure to toxins
1	Khaleel	M	17	59503	15	I	2	P	-	-	-	-	-
2	Ramasamy	M	54	100171	50	I	4	P	+	-	-	+	-
3	Sudhakar	M	19	59543	15	I	4	P	-	-	-	-	-
4	Jeevitha	F	18	77288	12	I	6	P	-	-	-	-	-
5	Vignesh	M	10	12267	8	I	2	P	-	-	-	-	-
6	Raji	M	24	23041	22½	I	1½	P	-	-	-	-	-
7	Naresh	M	20	76699	5 yrs	I	20	P	--	-	-	-	-
8	Maheswaran	M	23	94311	18	I	5	P	-	-	-	-	-
9	Amudha	F	34	78639	30	I	4	P	-	-	-	-	-
10	Sarath Babu	M	28	27816	21	I	7	P	-	-	-	-	-
11	Sudha	F	28	25494	22	I	6	P	-	-	-	-	-
12	Nirmala	F	47	56374	37	I	10	P	-	-	-	-	-
13	Vijayakumar	M	10	56369	8	I	2	P	-	-	-	-	-
14	Satishkumar	M	8	112778	2 yrs	I	6 M	P	-	-	-	-	-
15	Elumalai	M	41	102829	34	I	7	P	-	-	-	-	-
16	Udayakumar	M	24	39564	15	I	9	P	+	-	-	-	-
17	Murugesan	M	34	15472	31	I	3	P	-	-	-	-	-
18	Mohanakrishnan	M	16	44265	16	I	3 M	P	-	-	-	-	-
19	Tamilselvan	M	11	69774	5	I	6	P	-	-	-	-	-
20	Gnanaselvi	F	32	23818	27	I	10	P	-	-	-	-	-
21	Vinoth	M	15	44207	13	I	2	P	+	-	-	-	-
22	Murali	M	27	66114	20	I	7	P	-	-	-	-	-
23	Gunasekaran	M	16	81265	9	I	7	P	-	-	-	-	-

Sl.No.	Name	Sex	Age	OP/IP No.	HISTORY								
					Age at onset (Yrs)	Mode of onset	Duration of Illness (Yrs)	Progression	H/o Fatiguability	H/o Diurnal Variation	H/o constitutional symptoms	H/o Muscle Pain	H/o Chronic drug usage/ Exposure to toxins
24	Rajendran	M	47	31462	35	I	12	P	+	-	-	-	-
25	Prakash	M	19	43408	15	I	4	P	-	-	-	+	-
26	Haribabu	M	14	69824	7	I	7	P	-	-	-	-	-
27	Vinod	M	22	39352	19	I	3	P	-	-	-	-	-
28	Sneeha	F	12	102798	8	I	4	P	-	-	-	-	-
29	Ajith Fathima	F	53	58962	48	I	5	P	-	-	-	-	-
30	Devaraj	M	42	39503	32	I	10	P	-	-	-	-	-
31	Muniswaraiya	M	26	112314	23	I	3	P	-	-	-	-	-
32	Balaji	M	19	116379	15	I	4	P	-	-	-	-	-
33	Gunasundari	F	19	26355	18	I	1	P	-	-	-	+	-
34	Ramila	F	29	26836	26	I	3	P	-	-	-	-	-
35	Chandrasekar	M	23	12678	10	I	13	P	+	-	-	-	-
36	Vignesh	M	14	71870	13	I	1	P	-	-	-	-	-
37	Divya	F	20	22011	18	I	2	P	-	-	-	-	-
38	Sanjeevi	M	17	20201	14	I	3	P	-	-	-	-	-
39	Gowtham	M	17	18612	12	I	5	P	+	-	-	-	-
40	Kabali	M	14	61200	10	I	4	P	-	-	-	-	-
41	Dineshkumar	M	18	75201	16	I	2	P	-	-	-	-	-
42	Priya	F	17	40811	14	I	3	P	+	-	-	-	-
43	Raja	M	40	12207	35	I	5	P	-	-	-	-	-
44	Kavitha	F	30	130246	26	I	4	P	-	-	-	-	-

Sl.No.	WEAKNESS										PAST HISTORY	PERSONAL HISTORY			
	Symmetrical/ Asymmetrical	Proximal/ Distal/Both	Limbs UL/LL/Both	Trunk	Neck Muscles	Facial Muscles	H/o Breathlessness (Respiratory Mm)	H/o Thinning of Muscles	Exertion	Cold/Warmth	Similar Illness DM/SHT/HD/BA/ P.TB./SZ/Surgery	Smoking	Alcohol	Substance Abuse	Diet
1	S	Both	LL	N	N	N	N	Y	N	No Effect	N	N	N	N	Mixed
2	A	P	UL	N	N	N	N	Y	N	N	N	N	N	N	Mixed
3	S	Both P>D	Both	N	N	N	N	Y	N	N	N	N	N	N	Mixed
4	S	P	Both	N	Y	N	N	Y	N	N	N	N	N	N	Mixed
5	S	P	LL	N	Y	N	N	N	N	N	N	N	N	N	Mixed
6	S	Both P>D	Both LL>UL	N	N	N	N	N	N	N	N	N	N	N	Mixed
7	S	P	Both LL>UL	N	N	N	N	N	N	N	N	N	N	N	Mixed
8	S	D	Both LL>UL	N	Y	N	N	Y	N	N	N	N	N	N	Mixed
9	S	D	LL	N	N	N	N	N	N	N	N	N	N	N	Mixed
10	S	P	Both LL>UL	N	Y	N	N	N	N	N	N	N	N	N	Mixed
11	S	Both P>D	Both LL>UL	Y	Y	N	N	N	N	N	N	N	N	N	Mixed
12	S	Both P>D	Both LL>UL	N	Y	N	N	N	N	N	N	N	N	N	Mixed

Sl.No.	WEAKNESS										PAST HISTORY	PERSONAL HISTORY			
	Symmetrical/ Asymmetrical	Proximal/ Distal/Both	Limbs UL/LL/Both	Trunk	Neck Muscles	Facial Muscles	H/o Breathlessness (Respiratory Mm)	H/o Thinning of Muscles	Exertion	Cold/Warmth	Similar Illness DM/SHT/HD/BA/ P.TB./SZ/Surgery	Smoking	Alcohol	Substance Abuse	Diet
13	S	Both P>D	BothLL>UL	N	Y	N	N	N	N	N	N	N	N	N	Mixed
14	S	P	Both	N	N	N	N	N	N	N	N	N	N	N	Mixed
15	S	Both	Both	N	Y	Y	N	N	N	N	N	N	N	N	Mixed
16	S	P	Both	N	N	Y	N	Y	N	N	N	N	Y	N	Mixed
17	S	both	Both	N	N	Y	N	Y	N	N	N	Y	N	N	Mixed
18	AS	P	UL	N	N	Y	N	Y	N	N	N	N	N	N	Mixed
19	S	Both	Both	N	N	N	N	Y	N	N	N	N	N	N	Mixed
20	S	P>D Both	Both	N	N	N	N	Y	N	N	N	N	N	N	Mixed
21	S	P	Both	N	N	Y	N	N	N	N	N	N	N	N	Mixed
22	S	P	Both	N	N	N	N	Y	N	N	N	N	N	N	Mixed
23	S	P	UL > LL	N	N	N	N	N	N	N	N	N	N	N	Mixed
24	S	P>D Both	Both	N	N	Y	N	Y	N	N	N	Y	Y	N	Mixed

Sl.No.	WEAKNESS										PAST HISTORY	PERSONAL HISTORY			
	Symmetrical/ Asymmetrical	Proximal/ Distal/Both	Limbs UL/LL/Both	Trunk	Neck Muscles	Facial Muscles	H/o Breathlessness (Respiratory Mm)	H/o Thinning of Muscles	Exertion	Cold/Warmth	Similar Illness DM/SHT/HD/BA/ P.TB./SZ/Surgery	Smoking	Alcohol	Substance Abuse	Diet
25	S	-	-	N	N	N	N	N	N	N	N	N	N	N	Mixed
26	AS	P>D Both	UL > LL Both	N	N	Y	N	Y	N	N	N	N	N	N	Mixed
27	S	P>D Both	Both	N	N	N	Y	Y	N	N	N	N	N	N	Mixed
28	S	P>D Both	UL > LL Both	N	N	N	N	N	N	N	N	N	N	N	Mixed
29	S	P	Both	N	N	N	N	Y	N	N	N	N	N	N	Mixed
30	S	P	Both	N	N	N	N	N	N	N	N	Y	N	N	Mixed
31	AS	P	Both	N	N	N	N	N	N	N	N	N	N	N	Mixed
32	S	P>D Both	Both	N	N	N	N	N	N	N	N	N	N	N	Mixed
33	S	P	UL	N	N	Y	N	Y	N	N	N	N	N	N	Mixed

Sl.No.	WEAKNESS										PAST HISTORY	PERSONAL HISTORY			
	Symmetrical/ Asymmetrical	Proximal/ Distal/Both	Limbs UL/LL/Both	Trunk	Neck Muscles	Facial Muscles	H/o Breathlessness (Respiratory Mm)	H/o Thinning of Muscles	Exertion	Cold/Warmth	Similar Illness DM/SHT/HD/BA/ P.TB./SZ/Surgery	Smoking	Alcohol	Substance Abuse	Diet
34	S	P>D Both	LL	N	N	N	N	N	N	N	N	N	N	N	Mixed
35	S	P	LL>UL Both	N	N	N	Y	Y	N	N	N	N	Y	N	Mixed
36	S	P>D Both	Both	N	N	N	N	Y	N	N	N	N	N	N	Mixed
37	S	P	Both	N	N	N	N	N	N	N	N	N	N	N	Mixed
38	S	P	LL	N	N	N	N	N	N	N	N	N	N	N	Mixed
39	S	P	Both	Y	Y	N	Y	Y	N	N	N	N	N	N	Mixed
40	S	P	Both	N	N	N	N	N	N	N	N	N	N	N	Mixed
41	S	P	Both	N	N	N	N	N	N	N	N	N	N	N	Mixed
42	S	P	Both	N	N	N	N	N	N	N	N	N	N	N	Mixed
43	S	P>D Both	LL<UL Both	N	N	N	N	Y	N	N	N	N	N	N	Mixed
44	S	D	LL	N	N	N	N	Y	N	N	N	N	N	N	Veg

Sl.No.	FAMILY HISTORY	ON EXAMINATION								PATTERN OF MUSCLE INVOLVEMENT					
		Muscle Hypetrophy	Muscle Wasting	Muscle Fasciculation	Skeletal eformities	Contractures	Muscle Tenderness	Tone N/↑/↓	Toe/Heel Walking	Proximal Limb-girdle weakness	Distal Weakness	Proximal arm/distal leg weakness	Distal arm/proximal leg weakness	Ptosis with/without ophthalmoplegia	Prominent neck extensor Weakness
1	Autosomal Recessive	N	Y	N	N	Y	N	N	Toe Walking	+	-	-	-	-	-
2	Not clear	N	Y	N	N	N	N	N	--	-	-	✓	-	-	-
3	Not clear	N	Y	N	N	N	N	↓	--	+	-	-	-	-	-
4	Not clear	N	Y	N	N	N	N	N	--	+	-	-	-	-	-
5	Autosomal Recessive	Y	N	N	N	Y	N	N	Toe Walking	+	-	-	-	-	-
6	Not clear	N	N	N	N	N	N	N	--	+	-	-	-	-	-
7	X-linked recessive	Y	N	N	Pes	N	N	N	--	+	-	-	-	-	-
8	Not clear	N	Y	N	N	N	N	N	--	-	✓	-	-	✓	-
9	Autosomal Dominant	N	N	N	N	N	N	UL N LL ↓	--	-	√	-	-	-	-
10	No history	N	N	N	N	N	N	↓	--	+	-	-	-	-	-
11	Autosomal Recessive	N	N	N	Pes	N	N	N	--	+	-	-	-	-	-
12	No history	N	N	N	N	N	N	N	--	+	-	-	-	-	-
13	Not clear	Y	N	N	N	N	N	↓	--	+	-	-	-	-	-
14	X-linked recessive	Y	N	N	N	N	N	N	--	+	-	-	-	-	-
15	Autosomal Dominant	N	N	N	N	N	N	N	Toe Walking	+	-	-	-	P	-
16	Not clear	N	Y	N	N	Y	N	N	--	+	-	-	-	-	-
17	Autosomal Recessive	Y	Y	N	N	N	N	↓	--	+	-	-	-	-	-
18	No history	N	Y	N	N	N	N	N	--	+	-	-	-	-	-
19	X-linked recessive	Y	Y	N	N	Y	N	↓	--	+	-	-	-	-	-
20	Autosomal Recessive	N	Y	N	N	N	N	↓	--	+	-	-	-	-	-

Sl.No.	FAMILY HISTORY	ON EXAMINATION								PATTERN OF MUSCLE INVOLVEMENT					
		Muscle Hypetrophy	Muscle Wasting	Muscle Fasciculation	Skeletal eformities	Contractures	Muscle Tenderness	Tone N/↑/↓	Toe/Heel Walking	Proximal Limb-girdle weakness	Distal Weakness	Proximal arm/distal leg weakness	Distal arm/proximal leg weakness	Ptosis with/without ophthalmoplegia	Prominent neck extensor Weakness
21	Autosomal Dominant	N	N	N	N	N	N	N	--	+	-	-	-	P	-
22	Not clear	Y	Y	N	N	N	N	N	--	+	-	-	-	-	-
23	X-linked recessive	Y	Y	N	N	N	N	↓	--	+	-	-	-	-	-
24	No history	N	Y	N	Y	N	N	↓	--	+	-	-	-	-	-
25	Autosomal Dominant	Y	N	N	N	N	N	N	--	-	-	-	-	-	-
26	Not clear	N	Y	N	Y	N	N	↓	--	+	-	-	-	-	-
27	Not clear	N	Y	N	N	N	N	↓	--	+	-	-	-	-	-
28	Autosomal Recessive	N	N	N	N	N	N	N	--	+	-	-	-	-	-
29	No history	N	Y	N	N	N	N	N	--	+	-	-	-	-	-
30	Autosomal Recessive	Y	N	N	N	N	N	N	--	+	-	-	-	-	-
31	No history	Y	N	N	N	N	N	↓	--	+	-	-	-	-	-
32	Not clear	N	N	N	N	Y	N	N	Toe Walking	+	-	-	-	-	-
33	Not clear	N	N	N	N	N	N	N	--	+	-	-	-	-	-
34	Not clear	N	N	N	N	N	N	N	--	+	-	-	-	-	-
35	No history	N	Y	N	Y	N	N	↓	--	+	-	-	-	-	-
36	Not clear	N	Y	N	N		N	N	Toe Walking	+	-	-	-	-	-
37	No history	Y	N	N	N	N	N	N	--	+	-	-	-	-	-
38	No history	N	N	N	N	N	N	N	--	+	-	-	-	-	-
39	Autosomal Recessive	N	Y	N	Y	N	N	↓	--	+	-	-	-	-	-
40	X-linked recessive	Y	N	N	N	N	N	↓	--	+	-	-	-	-	-

Sl.No.	FAMILY HISTORY	ON EXAMINATION								PATTERN OF MUSCLE INVOLVEMENT					
		Muscle Hypetrophy	Muscle Wasting	Muscle Fasciculation	Skeletal eformities	Contractures	Musde Tenderness	Tone N/↑/↓	Toe/Heel Walking	Proximal Limb-girdle weakness	Distal Weakness	Proximal arm/distal leg weakness	Distal arm/proximal leg weakness	Ptosis with/without ophthalmoplegia	Prominent neck extensor Weakness
41	X-linked recessive	Y	N	N	N	N	N	N	--	+	-	-	-	-	-
42	Not clear	N	Y	N	N	N	N	↓	--	+	-	-	-	-	-
43	Not clear	N	Y	N	N	N	N	N	--	+	-	-	-	-	-
44	Not clear	N	Y	N	N	N	N	N	--	-		-	-	-	-

Sl.No.	GAIT	OTHER FINDINGS	INVESTIGATIONS							Provisional Diagnosis
			URINE MYOGLOBINURIA	SERUM CREATINE KINASE	ECG / ECHO	OPPHTHALMOLOGY	NERVE CONDUCTION STUDY	ELECTRO MYOGRAPHY	MUSCLE BIOPSY	
1	WG	AbN	Nil	3209	RBBB	-	N	Myopathic	M.D.	LGMD
2	N	AbN	Nil	105	N	-	N	Myopathic	M.D.	FSHD
3	WG		Nil	600	N	-	N	Myopathic	M.D.	LGMD
4	WG	AbN	Nil	1042	N	-	N	Myopathic	M.D.	LGMD
5	WG	AbN	Nil	3294	N	-	N	Myopathic	M.D.	LGMD with rimmed vacuoles
6	WG		Nil	745	N	-	N	Myopathic	M.D.	LGMD
7	WG	Gower's sign	Nil	5639	N	-	N	Myopathic	M.D.	?BMD
8	N	Hand grip	Nil	1261	N	-	N	Spont activity	M.D.	?Myotonic dystrophy Type I
9	N	-	Nil	986	N	-	N	Myopathic	M.D.	Distal Myopathy
10	WG	-	Nil	1106	N	-	N	Myopathic	M.D.	LGMD
11	WG	-	Nil	904	N	-	N	Myopathic	M.D.	LGMD
12	WG	-	Nil	1320	N	-	N	Myopathic	M.D.	LGMD
13	WG	Gower's sign	Nil	3347	RBBB Mild TR with RVH	-	N	Myopathic	M.D.	BMD
14	WG	Gower's sign	Nil	5885	N	N	N	Myopathic	M.D.	DMD
15	-	AbN	Nil	1080	N	N	N	Myotonic discharge	-	Myotonic dystrophy
16	Toe walking wadding	AbN	Nil	1877	N	N	N	Myopathic	M.D.	LGMD

Sl.No.	GAIT	OTHER FINDINGS	INVESTIGATIONS							Provisional Diagnosis
			URINE MYOGLOBINURIA	SERUM CREATINE KINASE	ECG / ECHO	OPPHTHALMOLOGY	NERVE CONDUCTION STUDY	ELECTRO MYOGRAPHY	MUSCLE BIOPSY	
17	WG	-	Nil	340	N	N	N	Myopathic	M.D.	LGMD
18	N	AbN	Nil	357	N	N	N	Myopathic	M.D.	FSHD
19	WG	Gower's sign	Nil	1800	AbN	-	N	Myopathic	M.D.	DMD
20	N	-	Nil	1330	N	-	N	Myopathic	M.D.	LGMD
21	N	AbN	Nil	590	N	N	N	Myotonic discharge	M.D.	Congenital myopathy
22	N	-	Nil	1135	N	N	N	Myopathic	M.D.	LGMD
23	WG	-	Nil	5239	N	-	N	Myopathic	M.D.	BMD
24	WG	AbN	Nil	407	N	-	N	Myopathic	M.D.	FSHD
25	N	AbN	Nil	625	N	-	N	Myotonic discharge	-	Myotonic dystrophy
26	WG	AbN	Nil	562	N	-	N	Myopathic	M.D.	FSHD
27	WG	Gower's sign	Nil	1345	N	-	N	Myopathic	M.D.	LGMD
28	WG	-	Nil	3410	N	N	N	Myopathic	M.D.	LGMD
29	WG	-	Nil	590	N	N	N	Myopathic	M.D.	LGMD
30	WG	AbN	Nil	1120	N	-	N	Myopathic	M.D.	LGMD
31	--	-	Nil	960	N	-	N	Myopathic	M.D.	LGMD
32	WG	-	Nil	8155	N	N	N	Myopathic	M.D.	LGMD
33	-	AbN	Nil	167	N	N	N	Myopathic	M.D.	FSHD
34	WG	AbN	Nil	434	N	N	N	Myopathic	M.D.	LGMD
35	WG	AbN	Nil	305	N	-	N	Myopathic	M.D.	LGMD
36	WG	-	Nil	1201	N	-	N	Myopathic	M.D.	LGMD
37	WG	-	Nil	510	N	-	N	Myopathic	M.D.	LGMD
38	WG	-	Nil	996	N	-	N	Myopathic	M.D.	LGMD
39	WG	AbN	Nil	356	AbN	-	N	Myopathic	M.D.	Congenital myopathy

Sl.No.	GAIT	OTHER FINDINGS	INVESTIGATIONS							Provisional Diagnosis
			URINE MYOGLOBINURIA	SERUM CREATINE KINASE	ECG / ECHO	OPPHTHALMOLOGY	NERVE CONDUCTION STUDY	ELECTRO MYOGRAPHY	MUSCLE BIOPSY	
40	WG	AbN	Nil	2100	N	-	N	Myopathic	M.D.	BMD
41	WG	AbN	Nil	1900	N	-	N	myopathic	M.D.	BMD
42	WG	-	Nil	953	N	N	N	mayopathic	M.D.	LGMD
43	WG	-	Nil	590	N	N	N	myopathic	M.D.	LGMD
44	High steppage	foot drop	Nil	498	N	-	N	myopathic	M.D.	Distal Myopathy

PROFORMA

Name: **Age:** **Sex:** **OP / IP No.:**

Address:

Mobile / Tel.No.:

History:

Age at onset :

Mode of onset :

Duration of illness :

Progression : Static / Progressive / Improving

H/o. Fatiguability : Present / Absent

H/o. Diurnal Variation : Present / Absent

H/o. Constitutional symptoms : Present / Absent

H/o. Muscle pain : Present / Absent

H/o. Chronic drug usage / Exposure to toxins

Weakness:

Symmetrical / Asymmetrical

Proximal / Distal / Both

Limbs : UL / LL / Both

Trunk : Present / Absent

Neck Muscles : Present / Absent

Facial Muscles : Present / Absent

H/o. Breathlessness(Respiratory Mm) : Present / Absent

H/o. Thinning of muscles : Present / Absent

Exertion : Worsens / Improves

Cold / Warmth : Worsens / Improves

Past History:

Similar illness / DM / SHT / HD / BA / P.TB / SZ / Surgery

Personal History:

Smoking	**:**	**Present / Absent**
Alcohol	**:**	**Present / Absent**
Substance abuse	**:**	**Present / Absent**
Diet	**:**	**Veg. / Non.Veg / Mixed**

Family History:

On Examination:

1. Muscle Hypertrophy	**:**	**Present / Absent**
2. Muscle Wasting	**:**	**Present / Absent**
3. Muscle Fasciculation	**:**	**Present / Absent**
4. Skeletal deformities	**:**	**Present / Absent**
5. Contractures	**:**	**Present / Absent**
6. Muscle Tenderness	**:**	**Present / Absent**
7. Tone	**:**	**Normal / Hypotonia / Hypertonia**
8. Toe / Heel Walking	**:**	**Present / Absent**

Power:

Upper Limb		Right	Left
Shoulder	ABD ADD FLEX EXT IR ER		
Elbow	FLEX EXT		
Wrist	FLEX EXT		
Handgrip			

Lower Limb		Right	Left
Hip	ABD ADD FLEX EXT IR ER		
Knee	FLEX EXT		
Ankle	Dorsiflexion Plantarflexion		
Toe Grip			
Neck Mm	FLEX EXT		

Pattern of Muscle involvement:

1. **Proximal limb-girdle weakness : Present / Absent**
2. **Distal weakness : Present / Absent**
3. **Proximal arm / distal leg weakness : Present / Absent**
4. **Distal arm / proximal leg weakness : Present / Absent**
5. **Ptosis with / without ophthalmoplegia : Present / Absent**
6. **Prominent neck extensor weakness : Present / Absent**

Deep Tendon Reflexes : BJ SJ TJ KJ AJ

Right :

Left :

GAIT :

Other Findings :

INVESTIGATIONS

Complete Blood Count :

Urine Routine Examination :

Urine Myoglobinuria :

Renal Function Test :

Liver Function Test :

Serum Creatine Kinase :

Thyroid Function Test :

ECG / ECHO :

Ophthalmology :

Nerve Conduction Study :

Electro Myography :

MUSCLE BIOPSY

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு:
பரம்பரை தசை நோய்களில் உடற்கூற்று சோதனை மற்றும் ஆய்வக பரிசோதனைகளை ஒப்பிட்டு மதிப்பிடுதல் பற்றிய ஆய்வு.

ஆராய்ச்சி நிலையம் : நரம்பியல் துறை,
இராஜீவ் காந்தி அரசு பொது மருத்துவமனை மற்றும்
சென்னை மருத்துவக் கல்லூரி,
சென்னை - 600 003.

பங்கு பெறுபவரின் பெயர் : உறவுமுறை :

பங்கு பெறுபவரின் எண். :

பங்கு பெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களைப் பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்குக் கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லாத எதிர்பாராத வழக்கத்திற்கு நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

இந்த ஆய்வில் எனக்கு இரத்தம், சிறுநீர், **Muscle Biopsy, EMG** பரிசோதனை செய்து கொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம்..... இடம்..... தேதி
கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம்..... இடம்..... தேதி

ஆய்வாளரின் பெயர்.....

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No: 04425305301
Fax : 04425363970

CERTIFICATE OF APPROVAL

To

Dr. N. Balamurugan
PG in DM Neurology
Madras Medical College, Chennai -3

Dear Dr. N. Balamurugan

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled "Correlative assessment of clinical profile with laboratory investigations in Hereditary Muscle disorders" No. 38062012.

The following members of Ethics Committee were present in the meeting held on 27.06.2012 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan, MD, FRCP, DSc.	-- Chairperson
2.	Prof. Pregna B. Dolia MD Vice Principal / Director , Instt. of Biochemistry , M M C, Ch-3	-- Member Secretary
3.	Prof K.M. Sudha MD Prof . of Pharmacology, MMC, Ch-3	-- Member
4.	Prof. C. Rajendiran, MD Director , Institute of Internal Medicine, MMC, Ch-3	-- Member
5.	Prof. Karkuzhali MD Director i/c, Prof of Pathology, MMC, Chennai -3	-- Member
6.	Thiru. S. Govindasamy . BA.BL	-- Lawyer

We approve the proposal to be conducted in its presented form

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee


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Correlative Assessment of Clinical profile
BY BALAMURUGAN NAGARAJAN 16101002 D.M. NEUROLOGY
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Correlative Assessment of Clinical profile with Laboratory Investigations in Hereditary Muscle Disorders
INTRODUCTION
Myopathies are disorders in which a primary functional or structural impairment of skeletal muscle exists.Muscle disorders are differentiated from disorders involving motor neurons,peripheral nerves or neuromuscular junction, by their characteristic clinical and laboratory features.Therefore, the approach to a patient with a suspected muscle disease is to determine the correct site of the lesion from history and physical examination. Once localized to the muscle, the next step is to identify whether the myopathy is due to a defect in the muscle channel, muscle structure, or a dysfunction in muscle metabolism. The next is to determine the cause of the myopathy.In general, Muscle disorders are classified into hereditary and acquired disorders.Finally, whether a specific treatment is available for that particular
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Correlative Assessment of Clinical profile with Laboratory Investigations in Hereditary Muscle Disorders INTRODUCTION Myopathies are disorders in which a primary functional or structural impairment of skeletal muscle exists.Muscle disorders are differentiated from disorders involving motor neurons,peripheral nerves or neuromuscular junction, by their characteristic clinical and laboratory features.Therefore, the approach to a patient with a suspected muscle disease is to determine the correct site of the lesion from history and physical examination. Once localized to the muscle, the next step is to identify whether the myopathy is due to a defect in the muscle channel, muscle structure, or a...